

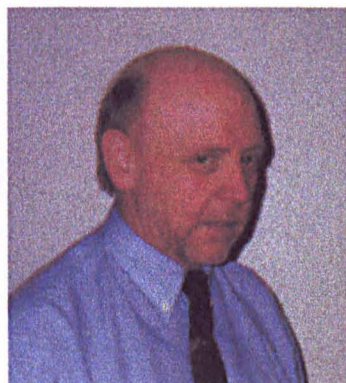
Electroanalgesia: Historical and Contemporary Developments

**A Thesis in Partial Fulfilment of
the Degree of**

Doctor of Philosophy

Vol I

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**Electroanalgesia:
Historical and Contemporary
Developments**

**A Thesis in Partial Fulfilment
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Philosophy**

Volume I

Sections 1-6

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Abstract:

Aims and Objectives: This thesis makes an in-depth examination of the historical, including the eighteenth-century pioneering electrical treatments of the Rev John Wesley, together with contemporary developments in electroanalgesia from the late twentieth-century, including the author's own pilot study, in order to provide a sound, scientific basis for their continuing use.

The problem and the hypothesis: Controversy still surrounds the effectiveness of electrical treatments, even after 250 years of application. This is seen in its most researched form as TENS (transcutaneous electrical nerve stimulation) and ALTENS (acupuncture-like transcutaneous electrical nerve stimulation) for chronic back pain. The empirical research making up the main part of the thesis sets out to provide clear evidence to reject the null hypothesis, i.e. that there are no significant clinical effects from the use of electrical treatments for chronic back pain.

Methods and findings: The empirical tertiary research centred on a systematic review and meta-analysis, within the framework of the Cochrane Collaboration, of all randomised controlled trials of TENS/ALTENS for chronic back pain found during rigorous searches of the medical literature. Pooling their results in a meta-analysis established that effective clinical benefits are to be found in the use of ALTENS/TENS for chronic back pain, at least in the short term.

Conclusions and recommendations: This wide ranging PhD thesis demonstrates for the first time significant clinical benefits of TENS/ALTENS for treating patients with chronic back pain and if implemented on a global basis, then considerable numbers of chronic back pain sufferers could benefit.

Acknowledgements

18th C View of the City site
of De Montfort University

All sections:

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Section 4.1-4.7:

To all members of the Cochrane Collaboration, too many for me to name them all, who have guided, taught and assisted me in many ways during the last few years of this research programme. To all members of the Collaboration who responded to my request for help in identifying non-English language publications of RCTS of TENS for chronic back pain, in twenty-six countries via the CCINFO Internet discussion list, operated by the Cochrane Informatics Project (CCIP) on behalf of the Cochrane Collaboration. Special mention too for Elena Telaro (Italian Cochrane Centre for help with translation and data collection of the Italian Studies). Finally, again with special thanks to Marilyn Bash of Body Clock Health Care Limited London, for assisting in the financial support of this project and the research programme in its entirety.

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Glossary of frequently used abbreviations:

		ModMan	Module Manager
AA	Acupuncture Analgesia	MPQ	McGill Pain Questionnaire
ALTENS	acupuncture-like TENS	NNT	number needed to treat
CD-ROM	Compact Disc - read only memory	OR	odds ratio
CDSR	Cochrane Database of Systematic Reviews	PAG	periaqueductal grey matter
CI	confidence interval	RCT	randomised controlled trial
CCTR	Cochrane Controlled Trials Register	RevMan	Review Manager
CRG	Collaborative Review Group	ROM	range of movement or motion
DARE	Database of Abstracts of Reviews of Effectiveness	RR	relative risk
EBHC	Evidence-Based Health Care	RRR	relative risk reduction
EBM	Evidence-Based Medicine	SG	substantia gelatinosa
EMBASE	Excerpta Medica database	TENS	transcutaneous electrical nerve stimulation
LBP	low back pain	TES	transcutaneous electrical stimulation
MEDLINE	MEDlars on-line	TNS	transcutaneous nerve stimulation
MeSH	Medical Subject Headings	VAS	visual analogue scale
		N.B.	See Appendix B (v) for the full thesis glossary

1. Summary:

The author of this doctoral thesis demonstrates the research process followed in order to encapsulate the historical and contemporary developments of electroanalgesia - from its earliest applications to the present day. The programme of tertiary research takes these objectives still further. Using a rigorous systematic review and meta-analysis, the author examined and established for the first time, the effectiveness of electrical treatments (TENS and ALTENS) in improving the symptoms of pain and restricted range of motion in chronic back pain patients. This study also investigated this subject area from both an orthodox physical therapy perspective as TENS and from the alternative and complementary viewpoint of ALTENS. This programme of study aimed to push back the frontiers of knowledge in the area of electroanalgesia in a significant way, and to this end, contains the following research elements, which together and individually contribute new and unique information to this knowledge base.

1. A history of medicine study, as a systematic review of the last 250 years of literature surrounding the Rev. John Wesley and his contributions to electroanalgesia, together with a wider view of his contribution to the development of alternative, complementary and holistic health care.
2. A randomised controlled trial of electroanalgesia in palliative medicine, which showed clinically significant effects in reducing the three most troublesome symptoms of the dying patient, pain, nausea and vomiting and fatigue. This study also demonstrates one way forward for researching physical (and other therapies), in order to assess the treatment effect of an intervention, over and above that of the placebo and the standard no treatment control.

3. A unique evaluation, in the form of a 'case study' approach, of the methodology of systematic reviews and meta-analysis targeted at new systematic reviewers especially those working in some isolation. This evaluation also examined the Editorial Review process, and how to challenge it if their findings were considered to be incorrect, together with an examination and evaluation of the new comments and criticisms mechanism of the Cochrane Library, set up in order to improve and update Cochrane Reviews.
4. A Cochrane systematic review and meta-analysis of the effectiveness of transcutaneous electrical nerve stimulation for chronic low back pain, demonstrating for the first time, the statistically significant effects of these treatments. This Cochrane review also became the first review, also linking together both orthodox and alternative/ complementary therapies, to be accepted for inclusion in the Cochrane Library under the Cochrane Musculo-skeletal Group – Back-subgroup section. Subsequently, during the process of improving the review, a cumulative meta-analysis was performed, which indicated that using TENS/ALTENS for the treatment of chronic low back pain could have been shown to be beneficial almost twenty years ago if this research had been done then.

This Cochrane Review was also externally validated a few months after publication in the Cochrane Library, by meeting the inclusion criteria for publication as a structured abstract and commentary in the Evidence-Based Medicine Journal (Gadsby and Flowerdew 1997) thereby making its unique contribution to the evidence-based health care literature.

2. Introduction

This thesis sets out the programme of research undertaken by the author for the degree of Doctor of Philosophy within the Department of Biological Sciences, School of Applied Sciences in association with the School of Health and Community Studies at De Montfort University Leicester, in order to evaluate the historical and contemporary developments of electroanalgesia. This in depth investigation and the critical development of the thesis was designed to 'push back the frontiers of knowledge' in this increasingly important conventional and complementary treatment area.

The aims and objectives of this research are:

1. To examine the historical developments of electroanalgesia in some depth by literature review.
2. To research by literature review, a history of medicine study of the Rev John Wesley's pioneering contribution to the development of electroanalgesia and an evaluation of the wider implications
3. To examine by literature review, the contemporary developments relating to the mechanisms of pain and electrical pain relief.
4. To research by empirical study, as a randomised placebo controlled clinical trial, the effectiveness of transcutaneous electrical nerve stimulation in the symptomatic treatment of cancer patients.

This first stage of the thesis was designed to set the electroanalgesia scene in some depth, to become experienced with the process of systematic literature searches, and to gain experience in the theoretical and practical applications of the research process, in preparation for the empirical research of the Ph.D. stage, whilst also making, at this stage of the programme, an original and unique contribution to our knowledge base in these defined areas.

The main aims and objectives of this next stage were:

1. To conduct an original piece of tertiary research, as a systematic review and meta-analysis in order to assess the effectiveness of transcutaneous electrical nerve stimulation in the treatment of chronic low back pain and to remove some of the controversies which still surround these methods of treatment even after more than twenty years of investigation and clinical application.
2. To produce a practical commentary, thereby extending the guidelines of the Cochrane Collaboration for the conduct of systematic reviews and aimed at novice reviewers seeking further information on the process, using a 'case study' approach.

The empirical tertiary research, as a Cochrane systematic review and meta-analysis, took up the vast majority of the research time and is original, in depth and does not replicate in any way preceding research or knowledge. Several literature reviews were identified (and evaluated in the thesis) during the search strategy, but this tertiary research study is the first and only systematic review and meta-analysis on the electrical treatment of chronic low back pain, which pushes back the frontiers of our knowledge base in this area, by evaluating all known randomised controlled trials as at January 1998.

In summary:

- The motives for this research programme at the doctoral level is to establish a sound evidence-base for the practice of electroanalgesia and to specifically establish whether the use of these treatments is scientifically valid for the treatment of patients with chronic low back pain.
- The main aims and objectives are set out above in order to provide this base and to answer the research questions relating to the electrical treatment of chronic low back pain.

- The null hypothesis was that these treatments are not clinically or statistically significant in the treatment of chronic low back pain patients. This study aims to show that we can reject the null hypothesis in favour of the positive evidence from a systematic review and meta-analysis of randomised controlled clinical trials.
- The research methods used and described in this thesis include literature reviews; randomised controlled clinical trials; systematic review and meta-analysis, the latter based on the methodological framework of the Cochrane Collaboration and the editorial process of the Musculoskeletal Group – Back Subgroup.

3.

**The
Historical and
Experimental Studies
Section of the
Thesis**

3.1 Introduction to the First Stage of the Study Programme.

This section sets the scene for the course of study with an in-depth examination of the electroanalgesia literature and a clinical research study of electroanalgesia in palliative medicine, designed to both help the dying patient and to gain experience in the research method, in order to form a solid basis for the doctoral level research stage in respect of the following areas:

- a. An examination of the historical background of electroanalgesia – from early beginnings to the present day (see 3.2).
- b. A history of medicine electroanalgesia case study from the eighteenth century based on the pioneer electrotherapist – The Rev. John Wesley MA (see 3.3)
- c. An examination of the biological and electrical mechanisms of pain and electrical pain relief (see 3.4 and 3.5)
- d. An electroanalgesia clinical research study- a placebo controlled randomized controlled trial of acupuncture-like transcutaneous electrical nerve stimulation in palliative medicine (see 3.6).

This randomised controlled study was designed with the aims of helping the dying patient in the following areas of palliative medicine:

- i. to improve pain relief,
- ii. to control nausea and vomiting,
- iii. to improve general fatigue symptoms
- iv. and to improve the overall quality of life.

with the aid of a well-designed and rigorous trial methodology.

The findings from this study were most promising for the future palliative treatment of terminally ill patients and for future researchers who may wish to build on these findings as described in section 3.6.

It was hoped that this piece of research could be developed into a full-scale powerful trial but the resources required were beyond the research team at the time of pilot study completion.

The conduct and findings of this pilot study also greatly enhanced the researcher's insight into the methodological aspects of the randomized controlled trial which was to prove invaluable during the later research stages of systematic review and meta-analysis as described in the Tertiary Research section of this thesis (see subsections 4.1-4.7).

3.2 Early Developments in Electroanalgesia

3.2.1 In the beginning.

The beginning of electrical stimulation for pain is coincident with the beginning of electrotherapy itself (Stillings 1975a). Though the origins of magnetism and electricity are lost, animated minerals such as amber, magnetite or lodestone were all known to ancient man. Starting around 9000 BC, bracelets, necklaces, and other appurtenances were used to prevent or assuage headache, arthralgia, and numerous visceral upheavals (Schechter 1971). Paracelus was enchanted with the properties of the magnetic stone and prescribed the lodestone with great abandon. However, much as the 'animated minerals' impressed the ancients, certain fish (Schechter 1971) inspired a yet greater sense of awe. For it is one of the curious symbolic coincidences that medical electricity can trace its origin back to the dawn of the astrological age of Pisces, and moreover, to a fish (Stillings 1973a).

Undoubtedly the first bioelectric phenomenon of which man became aware was the electric discharge of certain types of fish. Throughout the ages, electric organs in several species of fresh and salt-water fish, notably the *Torpedo mamorata*, *Malopterurus electricus* and *Gymnotus electricus* have reached a high degree of development and are capable of delivering a very painful and paralysing shock. These three species happen to be found near the sites of ancient civilizations, and it is probable that their uncanny power has been a source of fear and superstitious conjecture from very primitive times. The earliest man-made records in which electric fish are represented are the fishing scenes depicted on the walls of certain Egyptian tombs, C. 2750 BC. the electric fish represented being the Nile catfish, *Malopterurus electricus*. However in spite of the fact that its unmistakable lines appear in many early fishing scenes nothing has been extracted from the ancient inscriptions which throws any light on

what the Egyptians knew or thought of the electric catfish. There is no doubt, however, that the numbing force of the electric fish was known to the early writers and that the name was synonymous with the effect (Kellaway 1946).

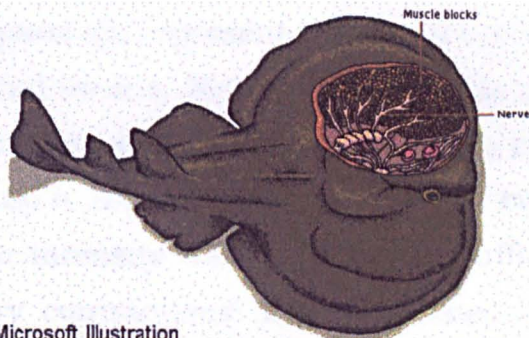
The first known Egyptian work to mention the electric catfish is dated some time in the 4th Century AD, in "The Hieroglyphica of Horapollo". The first chronicler was not concerned with the wondrous powers of these creatures but rather with their nutritive value. That the Hippocratic writings discuss the torpedo and yet make no reference to its strange powers is not remarkable, for these works are characterised by a rational approach to disease and an almost complete disregard for the marvellous and the esoteric. The simple prescription of easily digested torpedo flesh for the undernourished patient is merely another example of the Hippocratic belief in 'natural' therapy, and it stands in sharp contrast to the heavy-handed polypharmacy of succeeding ages (Kellaway 1946).

The torpedo fish was also well known to the fishermen working off the shores of the Mediterranean, before the birth of Christ, and numbing shocks were ample evidence that a torpedo had been ensnared in their nets. The saving and healing powers of fish were acclaimed throughout the medical and non-medical literature of the early centuries of the Christian era. These beliefs doubtless derived from the ubiquitous fish symbolism of the new religion and its founder, the Fisher of Men (Stillings 1973a).

On the basis of what can be garnered from the subsequent writings of Celsius, Oribasius and other compilers, it is apparent that nothing new was added to the medical history of the torpedo after Hippocrates (420 BC) until about AD 46, at which time the Roman physician, Scribonus Largus, introduced the electrical powers of the fish into clinical medicine as a cure for headache and gout. Of all the

amazing ichthyic nostrums by far the most remarkable, and perhaps the most rational was the employment of the torpedo's electric discharge for the relief of intractable headache and for gout. This remedy represents the first recorded use of electroanalgesia introduced into clinical practice. Historians characterize Scribonus as a man of sound judgement and high principles, his sole existing work being the '*Compositiones Medicae*'. He confesses that in his quest for remedies he gleaned from every likely person he encountered including slaves and wise women. Indeed he lists the electro-ichthyic remedy for gout on the basis of a report that Anteros, a freedman of Tiberius, had been successfully treated for the disease by this means (Kellaway 1946). After the initial excruciating cramp in his foot had abated, he found to his amazement that the pain he had long suffered, from gutta (gout), was completely banished. This event reached the ears of Scribonius Largus and his commentary appeared as follows.

For any type of gout a live black torpedo should, when the pain begins, be placed under the feet. The patient must stand on a moist shore washed by the sea (note precautions to keep the torpedo alive) and he should stay like this until his whole foot and leg up to the knee is numb. This takes away



Microsoft Illustration

present pain and prevents pain from coming on if it has not already arisen. In this way Anteros, a freedman of Tiberius, was cured. (Scribonius CLXII in Schechter 1971).

Scribonius gives no source, however, for the following description of his galvanic headache remedy and it is possible that he originated it himself (Kellaway 1946).

"Headache even if it is chronic and unbearable is taken away and remedied forever by a live torpedo placed on the spot which is in pain, until the pain ceases. As soon as

the numbness has been felt the remedy should be removed lest the ability to feel be taken from the part. Moreover several torpedo's of the same kind should be prepared because the cure, that is, the torpor which is a sign of betterment, is sometimes effective only after two or three" (Compositiones Medicae, XI. in Kellaway 1946).

The Herbal of Pedanius Dioscorides, '*De re medica*', written some thirty years after the '*Compositiones*', not only adopts the use of torpedo viva for headaches, (although this has been disputed by some - see Stillings 1973a/1975a), but avers that the remedy may also be successfully employed in prolapsus ani. This clinical application of electric fish is however left to the imagination of the reader (McNeal 1977). Largely through the influence of Dioscorides these remedies enjoyed a great popularity for many centuries and in fact may be found in herbals and pharmacopoeias up to the end of the seventeenth century, (e.g. in Robert Lovell's (1661) '*Panzooryctologica, sive Panzoologic-omineralogica*' p.191). One wonders if the electrotherapeutic treatments for prolapsus ani represent the first intentional stimulation of muscles by artificial means. Nicholas Godinho in 1615 observed that a live torpedo thrown among dead fish seemed to cause them to revive (Stillings 1973a). So it appears that the shock of even a dying torpedo is of considerable intensity and certainly of sufficient magnitude to induce involuntary contractions of semi-striated muscles in dead fish and live animals (Kellaway 1946).

The history of electricity in general medicine often refers to Claudius Galen's (131-201 AD) early use of shocks from the electrical fish to aid gout and other diseases and is on record as follows:

"The whole torpedo, I mean the sea-torpedo, is said by some to cure headache and prolapsus ani when applied.

I indeed tried both, and the torpedo should be applied alive to the person who has the headache, and that it could be that this remedy is anodyne and should free the patient from pain as do other remedies which numb the senses: this I found to be so, And I think that he who tried this did so for the above-mentioned reason." (Galen quoted in Stillings 1975/a).

Indian physicians of general medicine, for example, also employed them in all diseases characterized by excessive heat, and Ibn-Sidah, a Muslim doctor of the eleventh century, believed a live electric catfish to have beneficial effects when placed on the brow of a person suffering an epileptic fit (Kellaway 1946). Many others, until the end of the renaissance continued to cite recipes for the torpedo and its ilk. Marcellus Empiricus, Aetius of Amida, Alexander of Tralles, and Paulus Aeginata listed it among the specifics for various cephalgias and arthralgias. Serapion called it *Pisces stupefaciens*. The Arabians emphasised the virtues of the sleep, which followed the jolting contact with fish. Haly Abbas referred to the latter as the *Pisces dormitans*. Avicenna and Averhoes thought it efficacious when placed on the brow of persons afflicted with migraine, melancholy, or epilepsy. Persistence of this belief to the sixteenth century is exemplified by Dawud al Antaki's statement that:-

"If the torpedo is brought near, while alive, to the head of an epileptic, the latter will be thoroughly cured... it removes chronic headache, unilateral headache, and vertigo even in desperate cases" (Dawud al Antaki 16C in Schechter 1971/Stillings 1975/a).

So it appears that the use of the torpedo fish continued within general medicine and by the sixteenth century its application had

been broadened to include those suffering from migraine, melancholy and epilepsy (McNeal 1977). A 16th Century Jesuit missionary also described the use of electroichthic therapeutics as practised by the Abyssinians of that period in the treatment of arteries, joints and sinew pain. A seventeenth century traveller, Ludolf Hiob, also reported on the Abyssinians' treatment as follows:

"The Habessines cure Quartan and Tertian Agues with the torpedo, the patient is first to be bound hard to a table, after which the fish being applied to his joints, causeth a most cruel pain over all his members which being done the fit never returns again. A severe medicine which perhaps would not be unprofitable to those that are troubled with gout". (Ludolf Hoib in Kellaway 1946).

Instances of Europeans using electric fish as medical shocking machines are to found in the literature up to about 1850 (Kellaway 1946). Girolamo Cardano in 1551, and Gilbert one-half century later, by clearly differentiating between magnetism and electricity, laid the groundwork for the production and leashing of man made electricity to replace the piscine variety. Gilbert's crude electrostatic induction machines were archetypal of apparatus of that kind in use for the next three hundred years (Schechter 1971). The early years of the seventeenth century also produced two of the most important scientific works ever written: the 'De magnete' of William Gilbert (1600), which first generalised and classified the then known phenomena of electricity; and William Harvey's 'De motu cordis' (1628), describing for the first time (in the West) scientifically, the circulation of the blood (Stillings 1975a). However, Dr William Gilbert (1544-1603), who was also a court physician to Queen Elizabeth and to James the First, apparently never made any significant use of magnetic electricity, but the publication in 1600 of his experiments with the 'loadstone' earned

him the title of the 'First Electrician'. Belief in the medicinal properties of magnetism had been voiced by dozens of early writers including Albertus Magnus, Paracelsus, Discorides and Galen. While admitting the possible benefit of powdered loadstone and the possibility of using loadstone for removing arrowheads, Gilbert denied its value for curing headache and dropsy (Stillings 1974). Sixty years after the appearance of Gilbert's '*De Magnete*', Otto von Guericke in 1672, was the first to construct an early prototype of an electrostatic generator. He produced electricity by rotating sulfur against the friction of his hand (Stainbrook 1948). This effort being the first controlled artificial production of electricity.

Roughly coincident with the development of this electrotechnology, was the introduction of the practice of acupuncture, imported from Asia. In 1683, Ten Rhyne published his work '*Disser tatio de arthritide:mantissa schematica: de acupunctura...*', bringing the first details of oriental acupuncture pain relief to the West. Significant developments in electrical pain relief were found with the application of electricity to acupuncture needles in the early eighteenth century.

3.2.2 Electroanalgesia in the Eighteenth Century.

Hauksbee elaborated the crude implement of Otto Von Guericke further into an electrostatic generator, early in the eighteenth century (Stillings 1975a). Haukesbee's generator was a lathe and crank machine specifically designed for the efficient production of static electricity and he replaced von Guericke's sulfur globe with a glass one. His machine attracted the attention of Stephen Gray who has been credited with having laid the foundations for the study of electricity as a science (Stillings 1974). In 1742, Andreas Gordon, a Scotch Benedictine monk, replaced the glass globe with a cylinder and produced

the most powerful electrical discharges up to that time (Stillings 1974).

So long before the first treatises on the subject of medical electricity appeared on the continent, Englishmen had been methodically applying electricity to the body and reasoning as to its function in the animal economy (Stillings 1974a). But interest in electroanalgesia shifted from England to France during the middle years of the eighteenth century (Stillings 1974). Artificially generated electricity had begun to find favour with European physicians by the middle of the eighteenth century. Johann Gottlob Krueger, for example, in 1743 as the new professor of philosophy and medicine, first gave his 'Thoughts About Electricity' as a series of lectures in that year. These were published in 1744 and reprinted and 'enlarged by notes' again the following year. In a way, this was the first book on medical electricity, although the book of his pupil, Kratzenstein (1745), was the first to use medical electricity in a title (Licht 1959). Since the publication of this very first book on electrotherapy, the average output has been about five books each year (Licht 1959).

In 1745, Ewald von Kleist constructed the first electrical condenser; an achievement independently duplicated the following year in Leyden by Pieter van Musschenbroek (Stainbrook 1948). They developed a device that would both generate and store large quantities of charge. This was accomplished by the addition of the capacitor to the electrostatic machine. Nolan called this the 'Leyden jar', and used it in his experiments with animals and plants (Kane and Taub 1975). Christian Kratzenstein was probably the first physician to use the electricity from the Leyden jar for therapeutic purposes in general medicine (Stainbrook 1948). The medical applications of electricity, and especially indications for pain now multiplied rapidly (Stillings 1975a). Armed with the electrostatic generator and the Leyden jar, the electrical practitioners really went to work. Paralysis, hemiplegias, epilepsy, kidney stones, sciatica, and angina pectoris were only a few

of the conditions that were reported as successfully treated during the years that followed (McNeal 1977). For the invention of the Leyden jar permitted the use of far stronger shocks than the older static machines had been able to deliver, and called attention in a most dramatic manner to the effect of electricity on the human body. Between the years 1750 and 1780 no less than twenty-six papers dealing with medical electricity appeared in the *Journal de Medicine* alone. An electric shock machine, of the Ramsden type (glass plate style) was installed in the Middlesex hospital in 1767-8, and within the next decade many other hospitals followed suit. Almost immediately after the invention of the Leyden jar, however, the similarity between the shock it delivered and the discharge of the electric fish was pointed out, and physicians were quick to retest the remedial properties of the fish; apparently though, living shocking machines were seen as being more powerful than the man-made instrument (Kellaway 1946).

Storm van s'Gravesande, Governor of Surinam observed, in 1754, that various people who to some degree had gouty pains, and who touched the torpedo had been completely cured two or three minutes after contact. The experiment had been repeated at various times but always with the same result (Kellaway 1946). In 1761, a Dutch surgeon, van der Lott related 'experiments', also performed in Surinam with the ferocious Conger eel. It was noted that several black slave boys had been thrown into a tub of water, containing a Conger eel of the black variety, with subsequent improvement in the boys' 'nerve' condition and their fever (Schechter 1971). These remedies were much favoured by Indians and Negroes and they continued to use them until comparative recent times. For example, for many years the colonists of Berbice and Demerara made it a practice to keep two or three living *gymnoti* in a tank for the use of their plantation workers, who had great faith in the power of the fish's shock to cure rheumatic and paralytic afflictions. The Negroes were not alone in their faith for there are instances on record of European

doctors in Guiana using the shocks to treat rheumatism as late as 1850 (Kellaway 1946).

In Britain, Richard Lovett a lay clerk at Worcester Cathedral, claimed in 1755 to be successfully treating many conditions including mental disease by electric sparks and current (Stainbrook 1948). He published an account, the first English-language book on medical electricity, in 1756, of the many conditions for which electrotherapy was recommended, under the title '*The Subtil Medium Prov'd*'. John Wesley, the leader of the eighteenth century Methodist reformation, was so impressed by Lovett's electrical treatment that he enthusiastically observed in his own writings, in 1759, that:

"I doubt not but more nervous disorders would be cured in one year by this single remedy than the whole of the English Materia Medica will cure by the end of the century" (Wesley in Stainbrook 1948).

John Wesley's book, '*The Desideratum*' 1759, extolled the virtues of electricity in many diseases and its popularity can in some way be measured by the fact that the book went into its fifth edition by 1781. He believed so strongly in the therapeutic properties of electricity that he brought four machines to treat the people of London (Licht 1959). Wesley saw the 'subtle fluid' as the soul of the universe. He advocated electrical therapy for the following conditions:- angina pectoris, bruising, cold feet, gout, gravel in the kidneys, headaches, hysterics and memory loss, pain in the toe, sciatica, pleuritic pain, stomach pain, palpitations and so on. He ends his *Desideratum* with the following plea:

Before I conclude, I would beg one Thing (If it be not too great a Favour) from the Gentlemen of the Faculty, and in-

deed from all who desire Health and Freedom from Pain, either for themselves or their Neighbours. It is, That none of them would condemn they not know what: That they would hear the Cause, before they pass Sentence: That they would not peremptorily pronounce against Electricity, while they know little or nothing about it. Rather let every candid Man take a little pains, to understand the Question before he determines it. Let him for two or three Weeks (at least) try it himself in the above-named Disorders. And then his own Senses will shew him, whether it is a mere Plaything, or the noblest Medicine yet known in the World (Wesley 1759).

But compared with his position as the founder of Methodism, John Wesley's interest in electricity and his work as an electrotherapist are virtually unknown. Most of Wesley's applications would seem to many to be farfetched, but it is worth pointing out that Wesley's chief motivation for his promiscuous electrotherapeutics was his belief that this was an extremely effective cure that was, above all, cheap and therefore accessible to everyone (Stillings 1974a). The cataloguing of cases by Wesley in the above book, is evidence of the strictly empirical approach that dominated electroanalgesia in the eighteenth century. The wonder of sudden pain relief by discharging the marvelous electrical 'fire' through the afflicted body parts seemed to obviate any speculations regarding the physiology of the procedures (Stillings 1975a).

In the New World, theoretical electrical science was hardly a major concern of the early settlers in North America. Isolated from their families and traditions and faced with the day-to-day necessities of providing food and shelter, they could not ponder the niceties of natural philosophy. Even later, when the colonies began to enjoy a certain degree of prosperity, American science tended to produce

practical inventions rather than theories. Franklin was the exception to this rule, developing the one-fluid theory of electricity that was to hold sway over all others for more than a century. Still, Franklin himself was apologetic about not finding use for his discoveries, and when later did find one, namely, the lightening rod, the Americans considered it his most important scientific achievement (Medronic 1977). Benjamin Franklin, was at times besieged by the lame and sick with requests for electrotherapy. He was master of the science of electricity to that time and also one of the most vocal sceptics of the exaggerated claims of electrotherapists (Stillings 1974). No doubt Franklin's most important contribution to medical electricity was indirect: with his experiments he proved that electricity is an ever-present natural force; he developed the theory and terminology of positive and negative charge as well as the idea that a balance of charge is conserved in nature. Before Franklin, the study of electricity had been primarily a matter of philosophical speculation; after him, it became a science. Franklin removed much of the fear and superstition that had become associated with electricity, and in so doing, he opened the way to serious scientific investigation of electricity in the treatment of disease (Medronic 1977)

Back in Europe, Paris in 1772 saw the Abbe Bertholon using electrical stimulation for foot drop - *'in all such cases the stiffness of the tarsus is inconceivable'*. After warming the affected foot, he then applied continuous electrification for three-quarters of an hour, after which the patient was allowed to rest for a few minutes before the procedure was repeated for another three quarters of an hour (Stillings 1975b). In Britain, John Birch, an English surgeon, also in 1772, described the methods by which he applied electrical currents and gave case reports including treatment for injuries, low back pain, gout, constipation and other afflictions (Hymes 1984). However, despite the stories of success, there were many sceptics including Morin in France; Marrigues a surgeon at Montfort in 1773; and

Rabiqueau in 1782, an attorney, physics demonstrator, and optical engineer to the King of France; who failed to demonstrate the same degree of success (McNeal 1977). By 1777, more efficient machines were on offer, and as early as 1767/8 a machine had been installed at the Middlesex Hospital in London. St Thomas's, however, would not admit one until 1799, when John Birch finally prevailed:

"It was the usage at St Thomas's Hospital to admit nothing new into practice until seven years experience had given it validity. I have had three times seven years test of the pre-eminent power of electricity and am proud to own, that without this aid, I must have been obligated to perform many more operations" (Birch quoted in Licht 1959).

Meanwhile, towards the end of the 18th and during the first part of the 19th century, many specimens of '*Gymnotus electricus*' were exhibited in Europe. Due to the current popularity of electrotherapeutics, or Franklinism as it was then called, many people suffering from gout, rheumatism, and similar diseases flocked to try the curative power of the "natural" electricity discharged by the fish, and an advertisement published in London in 1777 invited one and all to come and be shocked by a "torporific eel" at two shillings and sixpence a time (Kellaway 1946). Learned and large volumes were also written on electricity in the second half of the eighteenth century by Cavallo and Priestley. In each, many pages were devoted to medical uses, for that remained its chief application before 1800. However, even before the nineteenth century began, interest in the application of static electricity in medicine had markedly diminished in Europe. Several magazines that had mentioned progress in electrotherapy each year made no mention of it following 1790. Communication of ideas was relatively slow, and the application persisted a little longer in America, where Gale up to 1805 was permitted to use

electricity on several convalescent yellow fever patients in Bellevue hospital (Licht 1959).

3.2.3 "Electro-quackery"¹ in the 18th Century.

One might suppose that 'quack' medicine would have tried to carve out a distinctive identity for itself through championing novelty, and, in an age of science and technology, patenting a wave of gadgets to bamboozle the public (Porter 1989). The late eighteenth century indeed, saw the invasion of the field by two notorious charlatans. In the UK, James Graham after meeting Benjamin Franklin in America became an enthusiast for medical electricity and gave lectures, demonstrations and expensive treatments with his 'Celestial Bed' and electrical instruments to ensure fertility (Licht 1959). Case histories from Bath and Bristol in the late 1770's show Graham offering electrical treatments for a spectrum of conditions, from the modish 'nervous diseases' to fevers, rheumatism, gout, deafness and noises in the head. In 1780 at the fashionable Adelphi in London, just off the Strand, he combined lectures and multi-media spectacle with a practice privileging electrical therapy. In this Valhalla of health and fertility, he first unveiled his celestial bed, hired out at £50 a night as a specific against impotence and sterility (Porter 1989).

"Electroquackery" in America had a history all of its own that was as long and colourful as that of legitimate electromedicine. The first great American fraud occurred shortly after the mesmerist cult took Europe by storm in the 1780's. The two bear a certain resemblance to each other in that they both were initiated by well-trained

¹ The author uses the terms "electro-quackery" and "quacks" with some reservation insofar as the references in this and subsequent sections of the thesis refer to the fraudulent use of electricity by medical and non-medical practitioners rather than their bona fide experimental applications of electricity for therapeutic uses.

physicians of great personal appeal, both promised quick and painless cures for disease, and both were mysteriously associated with that strange and marvellous new force, electricity (Medronic 1977). Elisha Perkins, with a medical degree from Yale, in 1796 secured a patent for 'electric' metallic tractors with which he claimed to cure many diseases by sweeping the skin with them. Glowing reports were published in the United States, England and Denmark, and it was not until 1800, when John Haygarth and Falconer of Bath, did a parallel control test with painted wooded tractors that the fraud was exposed. Even so, as has often happened before and since, Perkin's metallic tractors enjoyed considerable popularity for several years more (Licht 1959). For many years after the tractors fell from popular favour, America remained relatively free of 'electroquacks'. But the ideas were not dead, nor had electricity lost its appeal as a curative agent (Medronic 1977). However the grotesque proliferation of junk electrical technology - ozone boxes, masturbation-suppressors, electrical belts, thermal socks, hydraulic pimple squeezers, and the like - was a product of later Victorian 'quackery', (a reflex response, one suspects, to the introduction of laws regulating 'quack' pharmacy). So it would appear that Georgian 'quacks' probably drew upon the medical potential of electricity no more than their regular colleagues (Porter 1989) did. But did the 'quacks' colonise domains of disease relatively neglected by the regulars, such as intractable pain relief? Porter suggests not, for regular medicine did not trouble itself unduly about pain-control, and 'quack' medicine he suggests played not a pioneering role but rather followed in the footsteps of orthodoxy (Porter 1989). Graham's electrical therapy, for example, was integral to his overall medical doctrines and practice, and was, in any case, widely promoted by orthodox as well as 'quackish' practitioners in the last quarter of the eighteenth century (Porter 1989)²

² see Saks (1996) for a discussion on the issues surrounding quackery and complementary medicine.

3.2.4 Electroanalgesia in the Nineteenth Century.

The nineteenth century was the era of rational positivism - of faith in the individual, in the supreme power of human reason, in science as the key to understanding nature. Better educated and considerably more affluent, the public was no longer so easily taken in by the wiles of 'quackery'. The nineteenth-century charlatan had to sound like a scientist to gain a following. Medicine was changing from a mysterious, widely mistrusted profession into a science that relied on advance in physics and chemistry for its subsequent developments (Medronic 1977).

At the beginning of the 19th Century, however, the therapeutic use of electricity was contaminated by the prevailing ideas about animal magnetism, and the legitimate medicine of the UK and USA made little use of electrotherapy until after the beginning of the last half of the 19th Century (Stainbrook 1948). Also a clutter of synonyms marred the literature on electrotherapeutics for a couple of centuries. Their equivalents are herewith indicated; franklinization, the application of electricity generated by friction; galvanisation, the application of electricity generated by chemical reaction, the current so produced being designated as galvanic, voltaic, dynamic, continuous, constant, direct, primary, uninterrupted, battery, or pile (actually the galvanic current may be interrupted as well as the continuous) and faradization, the application of electricity generated in a coil of wires adjoining another conductor through which the current traverses. The faradic current, which is necessarily interrupted by the apparatus that produces it, is also referred to as induced induction, inductive, electromagnetic, magnetoelectric, to-and-fro, indirect, or interrupted (Schechter 1971). Alessandro Volta had produced the first battery (Voltaic pile) about 1799 and in 1801 Bischoff claimed to have cured hysterical paralysis and stupor by the application of the direct continuous current (Stainbrook 1948). The Voltaic pile was the first

source of electricity which could be produced without effort or regard to the weather, a current with characteristics so different from frictional electricity that for more than a half-century it was called galvanism in distinction from electricity, a name reserved for the static form (Licht 1959).

3.2.5 Electroanalgesia in 19th Century Britain.

By 1804, the galvanic current was being widely used for medical purposes in England for paralysis, tic douloureux etc (Stillings 1974). The London Electrical Dispensary at 16 Bunhill Street, founded in 1793, was able to report in 1820 that more than 8,000 patients had been treated there since its founding. Of these, 4,000 were listed as cured and another 3,000 as relieved. La Beaume was virtually the only physician interested in therapeutic electricity in England, but he was better appreciated in France than in his own country (Licht 1959:16). In 1836, Guy's Hospital set aside rooms for an electrical department and put Golding Bird, the instructor in physics, in charge. Because of his scientific standing, he soon had the co-operation of some of the leading clinicians of his time, especially Bright and Addison. However in some hospitals where electrotherapy was used the treatments were still entrusted to the house porter (Licht 1959). Bird gave lectures on medical electricity in 1847, which were published in 1849. These lectures had considerable influence (in the wrong direction!) which probably resulted in the Pulvermacher and Harness electric belts being foisted on a credulous public. These were the days of creativity in electrotherapy and many exorbitant claims often centring on improving the genital organs were proposed (Licht 1959).

Julius Althaus was the first in England to introduce the work of Duchenne, described later, and all other forms of electrotherapy. A graduate of Berlin, he settled in London in 1855 where he soon

began to administer electrical treatments at King's College Hospital (Licht 1959). In 1858 he applied 'interrupted' current transcutaneously to peripheral nerves. Althaus claimed like Garrett, that he had experimented with electrical anaesthesia long before Francis in America had popularised it. Whether this claim was true or not, Althaus was the major proponent of electrical anaesthesia in Britain and contributed a great deal to its dissemination (Kane and Taub 1975). He produced the first edition of his *Treatise on Medical Electricity* in 1859, and it reached its third, very much enlarged and revised edition in 1873. It is with this work that the era of purely empiricistic approaches to electrotherapy comes to an end (Stillings 1974). In subsequent years, the less careful, the less experienced, and the more cautious abandoned the technique of producing analgesia by electricity because of variable and irreproducible results. With its loss of popularity, obscurity followed, and it was necessary for 'local analgesia' to be 'discovered' (or rediscovered) many times after 1858, for example, Guyot in 1878, Araya in 1870-88, and others working in Chile at that time.

3.2.6 Electroanalgesia in 19th Century Europe

The nineteenth century witnessed a widespread irrational use of galvanism and of static electricity in Europe, which continued until the middle of the century when Duchenne and Remak, following Faraday's description in 1831 of electromagnetism, (and his first electric generator), and the subsequent introduction of the induced current, re-established the medical use of electricity on a more rational basis (Stainbrook 1948).

At about this time, something new was added to electrotherapy, which resulted twenty-five years later in the work of Duchenne. In 1821, James Morss Churchill's tract on acupuncture caused consid-

erable renewal of interest (Stillings 1975a). Acupuncture, or the treatment of disease by piercing the skin with needles, is an ancient practice of the Far East. Missionaries brought it back to France with them and Dujardin introduced it into the practice of that country in 1774. Berlioz revived it in 1811, and in 1816 suggested that the medical effects of acupuncture would be enhanced by electricity. Churchill's tract of 1821, also attracted the attention of Sarlandière, who in 1823 decided that all lesions of motion should be treated by (static) electricity and all those of sensation by galvanism. For him, the best way to introduce these currents was through needles. At first he practised electropuncture with both currents, but eventually he used only galvanism. Sarlandière claimed in 1825 that his method "introduces the shock into the very place I wish and this is able to modify the pain, motion or capillary circulation". He was convinced that he helped those with gout and arthritis (Licht 1959). Subsequently, Sarlandière published an extensive work on 'electroacupuncture' which chiefly discussed the great benefits for pain relief resulting from the combination of electricity and oriental needling (Stillings 1975a). He claimed at that time that electrical stimulation "confused" the perception of pain signals (McNeal 1977).

In 1820, Magendie in France, and Purkinje, also employed galvanic current to treat neuralgia, cardalgia and epilepsy (Stainbrook 1948). Later, in 1826, Magendie proved even bolder than Sarlandière and plunged platinum or steel needles into muscles and nerves. He then went on to introduce needles through the eyeball right into the optic nerve and then connected the needles to the poles of a battery. Magendie mentions his remarkable cures but not his failures or accidents (Licht 1959).

The man who probably did most to place electroanalgesia on a sound footing was Guillaume Benjamin Amand Duchenne of Boulogne, who started with the acupuncture of Sarlandière and Magendie

in 1833, but who later found that he could admit the electric current less painfully into the body with moistened surface electrodes (Licht 1959), this is also a popular 20th century method of electrotherapy application to be considered in detail later in this thesis. By 1849, Guillaume Duchenne was probably the first to use faradic current in medical research and treatment. Nonetheless the first results of his work was to stimulate in French medicine renewed interest in the galvanic current. Referring to Duchenne's experiments, Recamier in 1851, reported successful improvement in cases of obstinate constipation, abdominal pain and neuralgia's (Stainbrook 1948).

The attention to electrically produced muscular contractions led Duchenne in the 1850's to establish optimal or 'motor' points for electrode placement, a task to which Remak also made important contributions. Remak, in fact, did for German medicine what Duchenne did for medical electrotherapy in France, namely, re-established research in electrotherapy and electrodiagnostics as a valid scientific interest. Remak concluded from his observations on the therapeutic effects of electricity, particularly on the neuralgias, that inflammatory products were the cause of neuralgia and that the pathogenic factor was 'electrolized' by the galvanic current and so therapeutically altered (Stainbrook 1948).

Duchenne's book of 1855, *'De l'Electrisation localisee'*, was the major electrotherapy event of the century; it established electrotherapy (Licht 1959). In it, he proposed the use of faradic (induced) current, preferring it to galvanic current because of its electrolytic and warming action. He also introduced moistened pads to be used as surface electrodes, finding that they admitted electric current into the body less painfully than dry electrodes (McNeal 1977). The work of Duchenne was repeated in many countries including the USA, Hammond, who for a while was the

Surgeon General of the Union Army, used localised electrization on wounded soldiers in a Philadelphia Hospital (Licht 1959).

The analgesic effects of electrostimulation went on to receive wider recognition and acclaim throughout the nineteenth century especially in Europe (Stillings 1975a). In France, Hermel (1844), employed galvanic 'electro-puncture' for the treatment of sciatica and lumbo-sacral neuralgia, using two needles for electrodes and placing the positive needle-pole over the site of the pain. However, the method of 'galvanic acupuncture' was at the time a more common therapeutic procedure in Italy than it was in France, and it was used by Milani and Matteucci in the treatment of neurological diseases such as chorea, the various neuralgias and epilepsy (Stainbrook 1948).

Armed with a better understanding of electrophysiology and new devices such as the battery and the induction coil, electrical practitioners set off in pursuit of cures for diseases. The later half of the nineteenth century might be called the Golden Age of Medical Electricity (McNeal 1977). The Norwegian Engelskjøn, in 1855, treated hemicrania by electricity and based his selection of the kind of effective current upon his consideration that there were two essential forms of hemicrania, one being a disease of vasoconstriction and the other, a headache caused by vasodilation. Faradic current was used as an anti-vasoconstrictor, and galvanic electricity was employed as to constrict the pain-producing assumed vasodilation. Indirect support for this rationalisation of the electric therapy of hemicrania was derived from Engelskjøn's experience that those cases of hemicrania relieved by the inhalation of amyl nitrite also derived benefit from faradic current (Stainbrook 1948). In the 1860's headaches and neuralgia were frequently given electrical treatment, Brunelli, in the 1867 '*Gazzetta Medica Italiano*' reported a cure of spasmodic facial neuralgia with electricity after 18 sittings. Eulen-

berg in Berlin (1871) however, more carefully appraised the whole subject of the electrical treatment of the neuralgias and concluded that in the case of centrally produced neuralgia, a true cure by galvanism was doubtful and rare but that palliation of the pain was equally striking and frequent (Stainbrook 1948).

In 1883, the illustrious Wilhelm Erb wrote:

"At the present time we possess in the electrical current one of the most certain and brilliant remedies for neuralgia, although we must admit that much progress has not been made in our knowledge concerning its mode of action in these forms of disease (Stillings 1975a)

Bedwetting and 'sexual neurasthenia' also came within the province of 19th Century electrotherapy. Dommer in Germany (1898), for example, treated these conditions with reported partial success by passing faradic current between one electrode placed in the urethra and the other, in the rectum! (Stainbrook 1948).

3.2.7. Electroanalgesia in 19th Century United States of America

In America in 1802, Thomas Gale wrote a book, which indicated that the author had been practising electrotherapy since 1776, in New York State, and entitled: *'Electricity, or Ethereal Fire, Considered: 1st. Naturally, as the Agent of animal and vegetable life: 2nd. Astronomically, or as the Agent of Gravitation and Motion: 3rd. Medically, or its artificial Use in Diseases. Comprehending both the Theory and Practice of Medical electricity; and demonstrated to be an infallible Cure of Fever, Inflammation, and other Diseases: Constituting the best Family Physician ever extant'*. And that is just the title, the book goes on to extol the virtues of electricity and McNeal suggests that "in spite

of Mr Gale, or perhaps partly because of him, the initial flood of enthusiasm for electrotherapy began to wane toward the end of the eighteenth century in the USA and little serious work was attempted or reported during the first third of the nineteenth century" (McNeal 1977). Electricity then, was little used in American medicine in the early part of the nineteenth century. Even so, Brown of Troy N.Y., influenced by the reading of Wesley's '*Desideratum*' published a book on the subject in 1817. Although he was able to reproduce strong testimonials from prominent physicians whose patients he had treated, he was unable to influence other American physicians to engage in electrotherapy (Licht 1959). In 1858, Francis, a little known physician from Philadelphia, was the first to describe the relief of dental pain by electricity. He produced analgesia during a tooth extraction by the application of one electrode to the 'offending tooth' while another was held in the patient's hand.³ He described 164 successful tooth extraction's using 'galvanism', the majority of which resulted in 'no pain'. His 'controls', who received stimulation with the same set-up but with an open switch, did feel pain. A committee, appointed by the Pennsylvania Association of Dental Surgeons to study the use of electricity in dentistry, reported equivocal results, however, and did not recommend his apparatus for general use. Nevertheless, his technique spread almost immediately throughout America to Europe (Kane and Taub 1975). Garrett also recommended these techniques in peripheral neuralgias, hyperalgesias, tic douloureux and jaw ache etc, the electrodes being placed on the edge of the painful site for 3-5 minutes with just a bearable current. Oliver in 1857-8, in Buffalo, attached the negative pole electrode directly to the dental forceps. He also experimented with electrodes placed upon the limbs to produce surgically useful anaesthesia (Kane and Taub 1975).

³ The thesis author used the method on himself for a dental extraction of an upper molar tooth in 1996 and it gave him a very good analgesic effect.

George M. Beard assisted by Alphonse Rockwell (inventor of the electric chair), wrote their first book on the Medical Uses of Electricity in 1871. This was translated into German and went through ten American editions. Shortly after the publication of their book, Rockwell asked permission to present a paper on the subject before the New York Medical Society but was turned down on the ground that electrotherapy was advocated only by 'quack's (Licht 1959).

In 1872, a Dr Powell said:

There is nothing more striking in recent therapeutics than the change that has grown over the attitude of the profession in regard to the employment of electricity in medicine. Only 10 years ago to announce one's self a believer in electricity as a remedy of positive value was a hazardous thing (quoted in Licht 1959)

By 1875, Rockwell, Byrd and Rockwell published the second edition of their book that summarised the history of electrotherapy with long descriptions of its application. There were multiple chapters of specifics relating to system-related diseases, including asthma, rheumatism, gout, progressive muscular dystrophy, local motor ataxia, neuralgia, migraine and back pain. In addition, afflictions such as alcoholism, a variety of gastro-intestinal tract disorders, and skin diseases were also treated. A specific chapter on neuralgia and low back pain treated by electrical stimulation consisted primarily of case reports. Complications of chronic stimulation, such as scars and ulcerations of the skin, were also noted (Hymes 1984).

With the improvement in quality of static electricity machines in the latter part of the nineteenth century, they became increasingly popular and by the turn of the century most practitioners in America

had a static electricity machine in their offices. Typically American was the race to have the 'largest machine in the world' and it was eight feet tall and each of the eight glass plates was five feet in diameter. Electrotherapy reached its peak of popularity towards the end of the nineteenth century and it was used for everything. The journals of the day indicated its use from psoriasis in Moscow to neurasthenia in Philadelphia (Licht 1959).

3.2.8 "Electroquackery" in the 19th Century

So during the latter part of the nineteenth century, electricity rose to its greatest popularity as a therapeutic agent in Europe and America. But in addition to the dedicated medical men, the charlatan made his appearance too, making wild promises of health and beauty to a gullible public (Medronic 1977). The electric belt, for example, which appeared soon after the 'terrible tractoration' fad had died out, was destined for a less spectacular but much longer career. Originally developed in England in the 1870's, the Pulvermacher Electric Belt spread to the USA and enjoyed a degree of popularity throughout the latter part of the nineteenth century, although they never achieved the notoriety of some other patent devices of the period (Medronic). Interestingly, piscine electricity was still being used in orthodox and 'quack' medicine as late as the 1860's especially in Europe (Schechter 1971). However, the golden age of electrotherapy was coming to an end. Even though, as in 1890, Dr. J.B. Mattison called his colleagues attention to the value of Galvanism and Faradism for the relief of pain - neuralgic and myalgic, "*some of the best attested clinical facts that have ever gone into history have been along the line of Galvanism for relief of neuralgic pain*". But this appears to be one of the last testimonials to electroanalgesia, for after 1900, the use of electrical stimulation for pain is scarcely even mentioned in the literature, and a giant unexplained gap extends from that time to the present day (Stillings 1975a). However, static electricity retained

some of its popularity during the first quarter of the twentieth century and was not fully eclipsed until the advent of short wave diathermy (Licht 1959).

3.2.9 Electroanalgesia in the 20th Century

The early twentieth century brought many truly marvellous medical advances following the two previous centuries of electrical science which had shown great and continuous progress in the development of instrumentation and theory in electricity, and the credit for many fundamental accomplishments must go to British scientists. Even the colourful, if spotty, history of electroanalgesia revealed many possibilities, since the early inventors had few preconceived ideas about what electricity could or could not do, and in almost every instance a modern application of medical electricity can be traced to its eighteenth-century source (Stillings 1974). Nevertheless the piscine theme of electrotherapy which introduced this chapter remains of interest in the twentieth century, in that many primitive African tribes still employ the shock of *Malopterurus electricus* as a medicinal agent, a practice which is of very ancient origin and which may perhaps date from the time of the early Greek and Roman invasions of North Africa (Kellaway 1946).

3.2.10 Electroanalgesia in 20th Century Europe

The Golden Age of Electroanalgesia in Europe and Britain ended in the early twentieth century, probably for several reasons; the association with 'quackery' which had been established in the public imagination, the growth of the drug industry which competed for much the same market, and the appearance of x-ray treatments, had produced much more dramatic and documentable results than had

earlier electrical techniques such as electrographic diagnostic techniques (Medronic 1977 and Gadsby 1991;1993).

However the following exceptions are recorded: Peterson and LeDuc, (1902-3), rediscovered local electroanaesthesia at the turn of the century. Robinovitch in 1910, recommended local application of current in place of general anaesthesia, even for major operations using a modified LeDuc (interrupted D.C) technique. She found that optimal levels for anaesthesia were: 40V, 40mA peak, with pulse widths of about 1.0msec, and frequencies of 100imp/sec. With this arrangement, and with application of electrodes to appropriate nerves in the leg, several successful major lower limb amputations were performed in 1910 at St. Francis Hospital in Hartford (Kane and Taub 1975).

Hughson in 1922, Shaw in 1924, Guenot in 1953, also recognised the phenomenon of electrical anaesthesia but did not develop the interest further. Guenot recommended its clinical use but apparently did not employ it himself. Following the work of Thompson and Inman in 1933, Paraf in 1948 reported successful therapy in 127 patients with sciatic pain, lumbago, postherpetic neuralgia and tic douloureux. Guenot in 1953, described the work of Perrin, Barnard, LeGo, Presle, Wild and Prolest, all of whom used local and regional electroanaesthesia. Prolest experimented with 50-100 Hz monophasic and diphasic waves, which caused initial 'excitation' and paraesthesias, but soon caused 'inhibition' and raised the sensory threshold to the current (Kane and Taub 1975).

During World War I, there was considerable activity to hasten recovery of peripheral nerve injuries with electro-therapy. But this was a period of slow advance in electrical technology and virtually nothing new developed in the field then for many years (Licht 1959). During

field of physical therapy shifted to active participation by the patient and electroanalgesia rapidly diminished in importance, especially in Britain (Licht 1959).

Herin's (1968) study reviews the literature of electroanesthesia in great detail and concludes that, *"after weighing the pros and cons of electroanaesthesia, it is a tool which is not yet ready for the practitioner, except the research minded ones who want to use it on experimental animals"* (Herin 1968).

Local electrical analgesia as a phenomenon then lay dormant until its republication by Wall and Sweet in 1967 under the impetus of investigations originally initiated to study the effects of 'gating' peripheral input (Kane and Taub 1975). They reported temporarily abolishing chronic pain by electrically stimulating peripheral nerves via electrodes on the surface of the skin; the technique soon became known as 'Transcutaneous Electrical Nerve Stimulation (TENS)' (Wall and Sweet 1967).

3.2.11 Electroanalgesia in 20th Century United States

The early 1900's saw a proliferation of questionable therapeutic applications in the United States of America. This proliferation, coupled with an upsurge of promotion by paramedical and occult practitioners, brought about federal and medical society reaction so that many manufacturers of crude stimulators were forced out of business (Barr 1991). However, by 1900 most doctors in America had at least one electrical machine in their office, and what an array of machines there was to choose from (McNeal 1977). There were machines for pain relief in the arm; a tub for gouty or rheumatic feet; a stool for electricization by sparks; an electrostatic bath with cephalic douche; electrical poison extractors; Dr Karshner's electric baths with

douche; electrical poison extractors; Dr Karshner's electric baths with vaginal tubes and fountain; the solenoid cage; electrical belts - especially the Pulvermacher belt, described earlier, for weak and debilitated conditions of the generative organs; Dr Scott's Electric Hair Brush, at 1 Dollar, to prevent baldness, falling hair, dandruff and headache; electric tonics and so on. But electrotherapy again rapidly diminished in importance in the United States of America where it was regarded by some as old-fashioned (Licht 1959).

3.2.12 "Electroquackery" in the United States - Revisited:

It might be assumed that, with the passage of time, the increase in knowledge and knowledgeable people would make it increasingly difficult for a charlatan to establish himself, and to some extent this was true. Between the time of Elisha Perkins and Albert Abrams, more than a century later, there had not been a truly successful fraud in Medical Electricity in America. However at the beginning of the 20th Century, Albert Adams, a distinguished American professor of psychiatry recommended electrical treatments, based on a diagnosis which could be made only by the use of his secret machine, for which he charged physicians high prices in addition to a monthly royalty. The secret machine was analysed in 1925 and found to contain an electromagnet and a single turn of wire on a wooden disc but there was no complete circuitry. By 1925, it was estimated that hundreds of physicians in the United States alone were exponents of the system and as the books on Abrams treatments were also published in England, it is fair to assume that there were a few exponents here also (Licht 1959). Since the 1900's, a few manufacturers sold treatment machines such as the "Electreat" directly to consumers. These instruments became popular, and all imaginable types of claims, including the cure of cancer, were ascribed to these units, but the FDA banned their sale in the early 1950's (Hymes 1984).

3.2.13 Electroanalgesia in China.

So far the study has centred on the US/Europe axis, but no discussion on pain relief and electroanalgesia would be complete without a review of Chinese Traditional Medicine and their alternative theory of medicine, especially the use of acupuncture and electroacupuncture techniques. For acupuncture has been used in the treatment of pain and a variety of illnesses in China, and more widely in the Orient, for more than 2000 years. The practice of acupuncture is based on a theoretical system different from our understanding of human anatomy and physiology in the West and has developed through experience and observation. Stimulation of selective acupoints situated along 'meridians' is believed to restore bodily functions by promoting the flow of 'vital energy called 'Qi' throughout the system. Advances in technology in the twentieth century brought about new developments in acupuncture in China too and an electric current was first used with acupuncture in 1930. Although the early history of electroacupuncture may well be European (after Sarlandière 1825), it recurred in China in the late 1950's and spread widely throughout the country (Lu 1980). In 1958, Chinese physicians and anaesthesiologists began to apply acupuncture analgesia for major surgery. It was not long before electrical stimulation was found to be more convenient and effective than manual stimulation in many cases and the technique is in wide use today (Lu 1980). Electroacupuncture is also a rapidly developing field in the West too, as technologically minded orthodox and unorthodox practitioners rise to the occasion (Fulder 1989). This aspect of electroanalgesia will also be considered in detail later in this study.

3.2.14 Contemporary Electroanalgesia.

Following the demonstration by Wall and Sweet (1967) that stimulation of peripheral nerves in man produced control of pain, there was a new interest in stimulation as a potential pain control technique (Long 1991). Interest in the clinical application of electrical stimulation appeared higher then than at any other time in its history, wrote McNeal in 1977. Thousands of patients are being treated for chronic pain with both permanently implanted and non-surgically applied devices and without doubt, electrical stimulation will continue to play an important role in the future course of the field of medicine (McNeal 1977). Shealy and Long in the USA, were pioneers in this area of pain relief, initially using surgically implanted dorsal and anterior column electrodes for stimulation and later developing TENS in response to the observation that pre-operative TENS seemed to reduce the perception of pain almost as well as the dorsal column implant (Hymes 1984). While the original goal of transcutaneous stimulation was screening of patients for spinal cord stimulators, it became apparent quickly that stimulation of the skin was often sufficient to provide pain control alone (Long 1991).

The participation of private industry was an important factor in the early development of this rediscovered modality of TENS and these companies in the USA supported many of the studies. Secondly, the technical features of the instruments that were developed by these companies were an extremely important part of these investigations (Hymes 1984). The decade of the 80's produced more than 200 varieties of TENS and biofeedback devices and dozens of other pain-relieving modalities and techniques. Hymes writing in 1984 commented "it is interesting to note that electrotherapy had little use in the mainstream of modern medicine in the first 70 years of the 20th century in spite of the well-documented use of this modality in previous times". As such, little clinical research and few

publications have appeared in the medical literature until recently. Basic research, however, was being conducted (see Licht 1967) who reviewed the available historical literature and reported a comprehensive study citing more than 900 references. For the 20-year period from 1967-1987, Nolan (1991) compiled a bibliography of over 600 papers concerning TENS from clinical and basic science literature. In addition special journal issues and several books have been devoted to this subject (Barr 1991) and since 1967 an increasing number of orthodox and unorthodox health professionals have employed electroanalgesia, (TENS/EAP), in a wide range of acute and chronic pain conditions.

The efficacies of TENS/EAP, as a modality in the treatment of pain has now been well established, even if it cannot be seen as a panacea. It would appear that contemporary orthodox and unorthodox practitioners, over the last two decades, have rediscovered a modality that has been in the hands of various medical/other practitioners for the last two centuries or more. Although electrical stimulation was commonly used in the 18th and 19th centuries, reports were mainly anecdotal, often as case studies, and probably would not have withstood the critical, objective analysis demanded by 20th Century medical science. Albeit contemporary medical science itself is said to have only verified around 15% of its own contemporary clinical interventions (Smith 1991), partly because only 1% of the articles in medical journals are scientifically sound and partly because many treatments have never been assessed at all (Eddy quoted by Smith 1991). The main aim, therefore, of this programme of study is to strengthen the scientific bases of both conventional and unconventional electroanalgesic techniques as we head for the twenty-first century.

3.2.15 Discussion

From the mid 1700's, when investigators began meticulously to explore the effects of static electricity on the human body, to this century, when physicians routinely use electrical instruments to diagnose and heal, electromagnetism and the life sciences have been inextricably linked. Ideas from the past catalyze many of today's technological advances. But for all those ideas transformed into reality, many more still await exploration. Amongst them are important inventions waiting to be rediscovered, such as D'Arsonval's high frequency general anaesthesia. Electroanalgesia has itself been alternatively hailed as a panacea and damned as 'quackery' over more than two centuries of European and American medicine. So why did the 19th and early 20th century physicians reject these treatment methods? Quen (1975b) doubts that this rejection was based on simple selfish economics. Requiring no scientific training or knowledge, their widespread acceptance might have threatened the livelihood of the practising physician. It was also a confirmed observation, in the history of electroanalgesia and other methods such as 'Perkins Tractation', that electroanalgesia and 'Tractation' relieved patients, who had not been relieved by conventional treatments of the day (Quen 1963, 1964, 1975a). What factors in the medical and scientific communities determined the responses to these methods. Gunther Stent (1972) suggests that some scientific discoveries are premature because their implications cannot be connected by a series of simple logical steps to canonical, or generally accepted knowledge. This would appear to be the case with electroanalgesia and 'Tractation' theories that provided no acceptable rationale for the medical communities of the time. It appears that electroanalgesia was met with 'selective inattention' by the medical scientific community as in the case of Perkinism, or as nineteenth century Western acupuncture, receiving no theoretical explanation, was ignored by those who needed a 'normal science' rationale to allow themselves to acknowledge or use

it. We see then, a group psychological mechanism for rejection of those methods that do not provide an explanation. The absence of a scientifically orthodox theory of the mode of action, and the consequent implication of the imagination or the placebo effect are the dominant traits of these therapies according to the 19th and early 20th Century scientific communities (see also Saks 1995 for discussion of explanations). A situation which still persists to this day in respect of many alternative and complementary therapeutic interventions, if not in the case of conventional electroanalgesia in the form of TENS, it certainly does in the form of electroacupuncture as an alternative or complementary therapy. It is also an interesting observation that electroanalgesia and other treatment methods, rejected by the scientific medical community, provided relief and palliation for many people who did not benefit from 'normal science' medical treatment. Something was utilised, with apparently remarkable therapeutic efficacy, by the patients who responded to these anomalous methods (Quen 1975b). So today, the effects of electricity on the body are again the subjects of considerable interest among orthodox and unorthodox physicians and engineers alike (Medronic 1977) and that this interest is the motivating force behind this study. For if nineteenth century medicine was unable to distinguish between fallacious theory and therapeutic fact, are we really better able to do so at the end of the twentieth century? If not, which appears to be the case at the time of writing, then we must produce and publish strong research evidence to support, or reject, the theories and efficacies of electroanalgesia before we lose the methods yet again. I end this chapter with a quotation from D'Arsonval that I believe is as true today, nearly 100 years later, as it was then:

"I am convinced that the therapy of the future will employ heat, light, electricity and agents yet unknown. Toxic drugs shall cede their place to physical agents the employment of which at least has the advantage of not introducing

any foreign body into the organism” Arsene D'Arsonval,
1896.

In the course of reading for, and in the preparation of this section of the thesis, it became of increasing interest that the pioneering work of the Rev John Wesley had made a considerable contribution to electroanalgesia, not only in the eighteenth century but in the influence he had on its development in the centuries that followed. This early application of electrotherapy was well documented in his books, *'The Desideratum'*, *'Primitive Physick'* and also in his Journals. These writings show more than just a passing interest in this new treatment of 'electrifying' his sick followers. The next section (3.3), as a history of medicine case study, is devoted entirely to Wesley's pioneering work of healing the sick with an emphasis on his therapeutic use of electricity.

3.3 The Rev. John Wesley MA (1703-1791) Pioneer Electrotherapist: A History of Medicine Study



3.3.1 Introduction:

This section of the thesis examines the contribution of the Rev. John Wesley MA to health, holistic healing, and electrotherapy in the eighteenth century. A systematic review of the observations of twentieth century writers on his healing ministry and the use of electrotherapy is also presented. This enables us to make a fresh and original interpretation of his healing approaches, as seen in the light of the recent developments in holistic and alternative and complementary medicine during the last decade of the twentieth century. These specific aspects of John Wesley's healing ministry, seen from the viewpoint of a complementary medicine practitioner, have not been previously documented, although Wesley-Hill's (1958) work gives a most comprehensive study of Wesley's healing ministry from an orthodox medicine viewpoint. The study then goes on to examine the relevance and implications of John Wesley's healing work for both present and future research and the practice of electrotherapy and whole person medicine, both orthodox and unorthodox, as we prepare to enter the twenty-first century.

3.3.1.1 The life and times of The Reverend John Wesley MA:

John Wesley was born from thoroughly English ancestry, the son and grandson of Dissenting Church of England clergymen. His parents had, however, conformed to the Establishment before John was born. He was born in the tiny, isolated, marshy village of Epworth, Lincolnshire, in its Rectory, on June 17th, 1703. He lived almost throughout the whole of the eighteenth century and died on March 1st, 1791. He was the fifteenth out of eighteen or nineteen

children. He is said to have been 'methodical' as a boy, 'doing nothing without a reason'. Much has also been made of the story of his escape from the Rectory fire of 1709 and the belief that his mother impressed upon him that he was saved for some special destiny. He was certainly strictly brought up and his mother's guidance and influence were deeply marked in him (Rack 1993). John, at 17, after an education at Charterhouse, went to college at Oxford. He was ordained a deacon at 22 and a priest at 25 (Schiller 1981). John acted from time to time as curate to his father, until forced to reside mainly at Oxford, where he was for some years a Fellow of Lincoln College. He was seen as a man of great earnestness, strength of character and an indefatigable worker, but temperamentally more inclined to the cloister than to the parish (Baragar 1928).



As early as the spring of 1725, some months before his ordination, Wesley began to keep a shorthand diary, being then twenty-two years of age. Wesley's student life was not lacking in variety and he had an intimate acquaintance with men of social and intellectual distinction. The later Oxford Diaries and his published Journals show that during his residential university life he was a great traveller in the English counties, and often on foot (Curnock-footnotes 1909.1:7). From 1735-1738, he accompanied James Edward Oglethorpe to Georgia as a missionary among the colonists and the Indians. Following this period in America as a missionary, he returned home to his mother country to be shocked by the suffering of the poor people he found there (Dunlop 1964).

3.3.1.2 The development of Methodism:

The popular impression is that Wesley himself founded and organised the society of Oxford Methodists. Fertile in resource, it is assumed that he was a great organiser. It is more in accordance with facts to say that, however great he may have been in organisation, he

was not the originator. He utilised the experience of the past, borrowed freely from his contemporaries, knew how to follow a friend's initiative, and had a rare gift of assimilation. He was quick to see the usefulness of new ideas, and did not despise them because they came from other Churches or from friends and allies in his own circle. The class-meeting, lay preaching, and the love-feast are illustrations in point. Wesley, however, did not conceive the idea of the Holy Club, which appeared to be a spontaneous coming together of like-minded students - indeed, one of several such informal groups in Oxford at that time (Vickers 1996). He swiftly recognised the value of a simple institution into the founding of which men some years younger than himself had been led (Curnock 1909) and he did assume leadership at a later stage, largely by right of seniority and natural powers of leadership (Vickers 1996).

Methodist historians have naturally tended to emphasise the reasonableness and sobriety of their founder and followers and the social as well as the spiritual benefits they produced. The elements of irrationality and what some will see as religious hysteria in the movement have been played down. J H Plumb, in his 'Pelican History of England in the Eighteenth Century' suggests that "there was nothing intellectual about Methodism; the rational attitude, the most fashionable attitude of the day, was absolutely absent, and Wesley's superstitions were those of his uneducated audiences", quoted by Rack (1982) as an example of a rather wholesale dismissal of Methodism as a retrograde movement. However, earlier Plumb had allowed for more 'modernising tendencies in it' (Rack 1996). John Wesley could not then be considered a 'Rationalist' of the day, though rational he certainly was. Moreover, in Wesley's time according to Green, England was in a sadly degraded and corrupt state politically, socially, morally and religiously. The great masses of the poor, the common people, were "ignorant and brutal to a degree hard to conceive". For them there was little or no consideration from Church or State. Shocked

and stirred by this state of society, Wesley forsook the seclusion of Oxford Halls to bear to the miners and fishermen, and to the common people in general, a new religious life (Baragar 1928).

His zeal to teach Christianity on the long journeys which he pursued with tireless energy, brought him into contact with all conditions of men but he not only preached, he actually ministered healing and salvation. He saw the needs of men and women and met them head on (Maddocks 1988). His mission was to teach them how to live and this entailed looking after their physical as well as their spiritual needs. He was ever a keen educationalist and a publisher of around 400 cheap books and tracts for the general education of his people (including his preachers). *'Primitive Physick'* and the *'Desideratum'* described later were just two of a wide range of books he published including for example an English Grammar text. He also found health education lacking and supplied it, choosing his medical authorities with care and selecting from their remedies with discretion (Cule 1983). As he perfected the organization of the Methodist movement, he saw that he must meet a need, which the doctors of the day could not. His Journal describes the diffidence with which he started to provide medical treatment for members of the Methodist societies and the experimentation on both his patients and also upon himself (Andrews 1969). So the health and healing of the people to whom he ministered was also a part of his ministry (Maddocks 1988) albeit the salvation of their souls had a greater priority. Thus it is generally acknowledged that any attempt to assess the life and work of John Wesley must take into account not only his ministry to the souls of men, but also his concern for their bodies (Bowmer 1959).

3.3.1.3 Wesley's interests in health care:

Wesley at 21 may have been drawn to read Dr Cheynes work *'A Book of Health and Long Life'*, in order to find a cure for the severe

attacks of 'nose-bleeds' from which he suffered at this period of his life; his prejudice against the medical profession appears to have arisen in the first place on account of the unfavourable reception which Cheyne's work received at their hands (Turrell 1921). Wesley arranged his habits in accordance with the advice he found there, as well as in other medical works of either a popular or a technical character. We may concede, as his sarcastic biographer Robert Southey said, that he collected old women's nostrums (Dock 1915). Wesley believed, however, that a healthy body and mind went together with a redeemed soul, and he was a lifelong student of medicine. He read medicine with the same avidity he showed for theology and his bookshelf contained many well-thumbed medical texts (Dunlop 1964).

John Wesley's involvement in health care is documented throughout his writings. Early in his ministry Wesley established a visitation programme for the sick and dispensed medicine to the poor in London and Bristol. In 1747 Wesley published his collection of simple remedies under the title, '*Primitive Physick*'. He later procured an electrical apparatus by which he administered a form of therapy. In addition to these measures John Wesley urged his readers toward a life style conducive to good health. In his own early days he often lived a spartan life and he was always frugal, happy to adopt a simple daily diet and he certainly expected his preachers to make do on allowances providing for mere subsistence living. Wesley viewed a sensible regimen as the divinely appointed plan for a life of health as wholeness. His commitment to minister to the total person, an emphasis which antedates the contemporary interest in a more (w)holistic understanding of health, warrants an examination (later in this study) of those concepts critical to his view of health as wholeness (Ott 1989).

Like most eighteenth-century preachers, he was maligned for practising medicine. English pamphleteers protested repeatedly

against medical practice by clergymen of all denominations and distinctions (Rousseau 1968). However, the attacks on Wesley and his publications only began about 30 years after he first published his *'Primitive Physick'* and then continued throughout the nineteenth and twentieth centuries. Wesley seemed to take the early attacks upon his book in good humour. Of course, he was convinced the book was needed and its immediate and lasting popularity seemed to confirm its usefulness to those for whom it was intended. So we can understand Wesley's confident reply to one of his most outspoken medical denigrators, Dr. William Hawes, Physician to the London Dispensary: *"Dear Sir, My bookseller informs me that since you published your remarks on the Primitive Physick, there has been a greater demand for it than ever. If, therefore, you please to publish a few further remarks you would confer a favour upon Your Humble Servant"* (Wesley Hill 1958).

John Wesley practised medicine on his own authority and he did so because of the inadequate number of regular practitioners and the inability of the poor to afford medical treatment - even if they could obtain it (Cone 1978). Although he was concerned with the economic aspects of medicine in his age, he was also concerned with medical theory in his own time and with the general development and progress of medical science. He promoted the best medical advice of the day and the rules of the six 'non-naturals' - to be described later. Wesley, like the best medical thinkers of that period attributed most ailments to a violation of the six 'non-naturals' (Rousseau 1968).

3.3.1.4 Observations of twentieth century writers:

John Wesley's practice of medicine continued to fascinate the orthodox and unorthodox medical professions especially throughout the twentieth century, and the following observations are drawn from some of these publications, sometimes written in admiration, and sometimes in a disparaging style.

An early article in the BMJ, and written under the name of Nova et Vetera in 1902, examined the content of '*The medical tract of John Wesley*' with a descriptive review of his '*Primitive Physick*'. It covered the alphabetical listing of diseases and cures with an emphasis on some of the most bizarre and quaint, e.g. goose dung and celandine for a scirrhus of the mamma, but with less emphasis on those cures which had survived the nineteenth century, e.g. hydrotherapy, electrotherapy and naturopathic treatments (most of which have also survived the twentieth century too). The great majority of his 'Cures' are certainly 'Easy and Natural.' The same cannot unfortunately be said of some of the remedies of the faculty of that period (Nova et Vetera 1902).

A second article then followed in 1906, '*John Wesley on the art of healing*', also by Nova et Vetera. This article again outlined the structure and content and success of '*Primitive Physick*' but this time in more detail and in a somewhat disparaging style and ending with, "The medical profession may justly pride itself on the fact that it has made impossible the utterance of any such beliefs by any educated man of the present generation" (Nova et Vetera. 1906).

'*The Primitive Physick of Rev. John Wesley*' by Dr George Dock is an article quoted by many of the twentieth century writers. 'A picture of eighteenth century medicine' is the article's subtitle and contains an account of Wesley's contribution to health care, together with the contribution of leading physicians of that time. This article is more sympathetic to Wesley than the earlier ones. Dock was strongly impressed by the strange combination of good sense and superstition that gave him an insight into the conditions under which it was composed. He considered an analysis of such a work would have interest as both recalling an almost forgotten period of medicine and as an index of more modern conditions. Thoroughly as Wesley believed in some mystic forms of treatment, and firmly as he believed in the su-

pernatural as he viewed it, he did not mix his medicine with religion, for his recommendation of prayer in treatment is very mild (Dock 1915), but certainly not absent!

Stillings, in 1973 and 1974, reviewed the philosophy of electricity, presenting some of Wesley's highly metaphysical notions of the nature and function of electricity and also his practice as an electrotherapist. He ends by saying that "Most of Wesley's applications of electricity would seem to us to be very farfetched [an observation that will be examined later], but it is worth pointing out that Wesley's chief motivation for his promiscuous electrotherapeutics was his belief that this was an extremely effective cure that was, above all, cheap and therefore accessible to everyone" (Stillings 1974).

3.3.1.5 Principles and Practice of eighteenth century medicine:

In the seventeenth century the strengths and weaknesses of 'learned medicine' for those who could afford it were still those of the medicine of Antiquity, particularly that of Galen, on whose authority it leaned so heavily. It set great store by the management of a healthy life through the regulation of diet, exercise and the pursuit of moderation. The accent of its therapeutics lay on expelling toxic substances from the body (by purgation, procuring sweating and vomiting and the much favoured technique of 'blood-letting'), on restoring 'balance', and on strengthening the body's own regular constitution; to this end a host of medicaments was used (Porter 1987).

That ignorance and error are largely responsible for man's woes, including most of his physical ailments, is also an ancient doctrine. Our intemperance draws incurable diseases down upon our heads, and physicians will tell you that it is in offending in some of the 'six non-natural things' that lie the causes of our infirmities. There are six categories of factors, which operatively determine health or disease,

depending on the circumstances of their use or abuse, and human beings are unavoidably exposed to these in the course of daily life. They are: air; food and drink; sleep and watch; motion and rest; evacuation and repletion, the passions of the mind. Management of the regimen of the patient, that is, of his involvement with these six sets of factors, was for centuries the physician's most important task and has of course by no means lost its importance today (Rather 1968).

In addition to this concept of the 'six non-natural things' the work of Dr George Cheyne also had a significant influence on John Wesley. His voluminous writings represent well the intellectual activity of his era. Much of Cheyne's practice, especially his therapeutic concern with a 'low' diet was dictated by his own personal experience of gross obesity. His theories reflect the intellectual movements and conflicts of the period. Scientific achievements had little effect on the people; traditional religion, however, affected their lives quite directly. Soul and mind, as material entities, had to find a place in the philosophical explanations and systems of medicine and the biological sciences (King 1974).

The concept of obstruction played an important part in 18th century medicine. Cheyne's concept of disease reflected the then current thinking in physiology - that bodily processes depend on the free passage of fluids (or humours) through vessels of various types. Other factors, however, would also play a part such as the concept that food introduces an excess of tartarous, urinous or other salts into the blood, which when not properly broken down by the digestive process, unite in clusters to cause obstructions. Evacuations help to eliminate these salts. Cheyne held strongly to this type of therapy - at least in the form of gentle sweats and purges. Mineral waters and tea act as dilutents which thin the blood and 'dissolve and break the salts and keep them from running into clusters.' Mercury also had great merit

in relieving obstruction, being fourteen times as heavy as water, and thus having great force in 'opening' obstructions (King 1974).

3.3.1.6. Medical training and practice:

At the start of the 18th century the population of England and Wales was about 5.5 million; by the end of the century it had increased to nine million. During this period only a few graduates emerged from the nation's medical schools each year. Oxford provided four graduates a year; Cambridge usually supplied a few more. Edinburgh, then the centre of medicine in the English-speaking world, sent out as many as sixteen, and most people lived and died without ever seeing a doctor (Wilder 1978). Other doctors learned their profession by reading medicine or serving as apprentices under established physicians. There was also a strange and pernicious array of quacks practising in the land, and Wesley often protested against their influence upon the poor and ill educated (Dunlop 1964).

The first half of the 18th century, and much of the second half, continued the tradition that had long dominated academic medicine, namely that logic was more important than observation, and that theory derived its force more from internal consistency than from empirical verification. Progress towards a more modern viewpoint came slowly, only after medicine accepted new standards of evidence, new criteria for validity, new evaluations of cogency (King 1974).

3.3.1.7 Other 18th Century health care practitioners

Many fields of irregular medicine were actually growing alongside the rise of regular physic, and the eighteenth century has been called 'the golden age of quackery'. To speak of 'quackery' is not automatically to impeach the motives of empirics, i.e. unqualified practitioners and nostrum mongers, nor to pass judgement on their cures

as necessarily ineffective. Many proprietary remedies were remarkably similar to those prescribed by physicians, such as opium for pain and antimony to induce sweating, but other treatments were seen as entrepreneurial (or as unwarranted interventions), e.g. electric shocks (Porter 1987).

There were many, wise women and men alike, who made a good living from irregular medical practice. Many clergymen of that day also dabbled in physic, including Wesley's own grandfather who, when deprived of his living through politics, turned to the practice of physic (Baragar 1928). The regular physician, whose hard-won medical degree represented many years of intense study, looked down upon other groups; but only when financial matters intervened did this disdain change to intense opposition. The apothecaries were less well educated and had learned by apprenticeship and practical experience. The empirics stressed the facts of observation and considered these to be of primary importance, acquiring knowledge from chance observation and/or deliberate experimentation.

There were other individuals, such as the gentry and clergy, eminent men of the highest stature, neither physicians nor apothecaries, who were in no sense 'quacks', but who may also be called medical empirics (using trial and error in practice) in the best sense (King 1958). John Wesley was one of these and he also argued that medicine was formerly based on experience, until men of learning began to set this experience aside, to form theories of diseases and their cure, and to prefer these to experiments. Wesley's views are therefore superb examples of that school of medical theory known as 'Empiricism', i.e. that medical knowledge must be based upon experience, not upon theory (Callaway 1974). Obviously, today, we acknowledge that both theory and experience are necessary. In the 18th century, both extremes were being argued by capable but often hostile camps. The theorists have gained the approbation of history, since they were our

direct scientific ancestors but in the 18th century, neither camp could treat sick patients reliably. The Empiricists at least had centuries of trial and error on their side (Callaway 1974).

Wesley had set up an empirical system that, if we judge by popularity alone, worked at least as well as its more orthodox rival (King 1958). Wesley also awakened an interest in sanitation (and health promotion), long absent from the Christian world, with the revival of an ancient Hebrew dictum that 'cleanliness is next to Godliness' (Ott 1980a). In many ways the system of John Wesley was ahead of current medical opinion - he deprecated those dreadful eighteenth century panaceas - bleeding, blistering and purging. He actually believed that fresh air was helpful, and that cleanliness was next to godliness, ("the bath becomes still more efficacious by dissolving some soap in it"). He also spoke out against the complicated, useless and at times revolting formulations often containing 15-20 ingredients, that were in vogue at the time (Menzies 1980), in favour of simple single and less toxic remedies.

3.3.2 'Primitive Physick' (1747)

A combination of basic concerns - the maltreatment of the poor, the general incompetence of medical practitioners, and the innate greed of mankind in general - becomes the principal motivation behind the volume (Rogal 1978) of John Wesley's *'Primitive Physick, or An Easy and Natural Way of Curing Most Diseases'*, which was published anonymously in 1747. Among Wesley's chief concern as a bookseller was to make books affordable, *Primitive Physick* was so cheaply printed that it was among the dozen or so most widely read books in England from 1750-1850 (Brantley 1984). The book sold at a price low enough that even the poor could buy it (Dunlop 1964); for example it sold for one shilling in July 1747, a cheap price even then (Rousseau 1968). The total number of copies printed is unknown, but

it must have been one of the all-time medical best sellers (Stewart 1969), and unlike the dozens of other similar works written in the eighteenth century, it contained remedies for virtually every disease known to man (Rousseau 1968). In Wesley's lifetime it went through twenty-three editions and subsequently reached its thirty-second edition.

The first part of the book consists of a preface, to which are appended rules for the preservation of good health. The second part, (1780 Edition), consists of over nine hundred recipes and directions for two hundred and eighty-eight named ailments (Wesley Hill 1958). Extremes of good sense and nonsense are found among these 'receipts' although its author intended it to be a shield against quack medical practice (Dunlop 1964). Some of the remedies proposed are simple enough, none can deny; many are calculated to be beneficial; whilst the employment of a few, to say the least, would be extremely perilous (Stamp 1845). Wesley probably knew as much as most members of the medical profession, in fact, on no less than twenty instances throughout the volume, he paraphrases or cites directly from prominent physicians and theorists - such figures as Sydenham, Boerhaave, Cheyne, Mead, and Huxham (Rogal 1978). The majority of his cures were hardly original, but taken from the major medical figures of his time, together with folk medicine, old women's nostrums and some cures of his own invention. For the most part, Wesley's suggested remedies were simple, easily understood, inexpensive, and safe. Cold water, hot poultices, herb teas, and general hygienic measures were his standard treatments. Although many of the remedies are quaint by modern standards, they are much less bizarre than most other eighteenth century recipes (Menzie's 1980).

Despite the contributions of the leading physicians of the day, Wesley thought that their advancement of anatomical, physiological, and pathological theory added little to medical therapeutics (Dunlop

1964) and so his book of '*Primitive Physick*', by which he meant to imply a return to the simplicity of tried remedies in place of those of medical philosophers, who substitute theory for experience (Cule 1982), was his attempt to redress the balance. Wesley felt that cures can and should be discovered by accident and that discovering cures and experimenting with them was the primitive way by which was gathered up the whole corpus of healing (Payne 1985). However, he also includes the following caveat in '*Primitive Physick*', "that in uncommon or complicated diseases, where life is more immediately in danger, every man without delay should apply to a Physician that fears God" (Wesley 1747). This, however, did not keep him from advocating his own empirical cures for lesser ills, and throughout his life he sought for medical knowledge where he could find it (Dunlop 1964).

It was not until 1760 that Wesley's name appeared on the title-page. In this edition, too, he added 'Tried' to those remedies which he had found to be of greatest efficacy, and enthusiastically commended electricity as coming "the nearest an universal medicine, of any yet known in the world" (Wesley 1760). The "tried remedy" has a lasting appeal and the very term itself creates its own authority. It was what John Wesley often meant when he referred to a good result being "shown by experiment", but which nowadays is usually expressed as "shown by experience" (Cule 1990).

3.3.2.1 The preface:

Wesley's very long preface summarises the history of medicine from the earliest times to the present, with primitive man living in his perfect creation and suffering no sickness until his blissful state was marred by original sin, which then sired all diseases (Rousseau 1968). The preface goes on to offer down-to-earth rules covering diet, fresh air, exercise, sleep and cleanliness, rules for good health which would

need only moderate up-dating to be useful today (Stewart 1969). For example, 'In the sweat of thy face shalt thou eat bread, till thou return to the ground' - Wesley's interpretation indicating that 'the power of exercise both to preserve and restore health is greater than can well be conceived, especially to those who add temperance thereto' (Wesley 1747). Another example is his express belief that too much sleep may be the cause of many disorders, particularly nervous disorders. He exhorted, "You have no other possible means of recovery, in any tolerable degree, your health both of body and mind, Do not murder yourself outright" (Wesley 1831). As for the relationship between too much sleep and disorders, Wesley could only theorise (Ott 1980b). Nevertheless it seemed to John Wesley that "while we sleep all the springs of nature are unbent," and if we sleep longer than is necessary, "they (i.e. the springs) are relaxed more than is sufficient, and of course, grow weaker and weaker" (Wesley 1831). It is most interesting that recent sleep research suggests many similarities between excess sleep states and chronic fatigue syndromes such as Myalgic Encephalomyelitis (Horne 1995), and perhaps time may also show that a return to John Wesley's regimen recommendations for sleep may be the answer to this twentieth-century problem, i.e. that men require on average just six to seven hours of sleep and women seven to eight hours (Wesley 1831). The preface follows on with his understanding of what is now called psychosomatic or stress-related conditions, which was extraordinary for his day. "The passions have a greater influence on health than most people are aware of," he wrote and, "Till the passion, which caused the disease is calmed, medicine is applied in vain" (Wesley 1747).

Although many of Wesley's specific remedies now seem quaint, humorous, and, at times, grotesque, the moral force of his preface remains alive. In his critique of 18th century medicine, Wesley attacked not merely the 'fine spun theories' of the physicians of his time. More significantly, he attacked their arrogance, their desire to become

'something more than Human,' their avarice, and their abstruseness - vices that have by no means disappeared for the medical profession today (Callaway 1974).

3.3.2.2 A Collection of Receipts - the remedies:

The second part of his book presents 900 recipes and cures for 288 afflictions from abortions to wounds (Dunlop 1964). Its recipes were laid out alphabetically in the manner of a dictionary, and listed in simple English seven or eight - sometimes more - cures for each ailment; there was nothing 'scientific' about it according to Rousseau (1968). The recipes within *Primitive Physick*, though exciting the mirth or scorn of many twentieth-century observers, were in fact carefully selected by Wesley and represent the elect of eighteenth-century prescriptions for the purposes mentioned and form a basis for assessment of what was the best in eighteenth-century medical treatment (Wesley Hill 1958). He generally provides several remedies, which he recommends should be tried in order, if necessary. He realised that not all were easy to obtain, and that what cured one would not always cure another (Payne 1985). There is a relaxed, familiar, uncomplicated quality about the book. It is innocent of diagnostic hints so that the user of the book is directed toward the symptomatic relief of chronic, rather than acute disorders. The word 'cure' is tossed about carelessly, and the user of the book could find great room to manoeuvre (Stewart 1969). Though he was still a son of the 18th century and its superstitions, he was ahead of his time in many ways, (Dunlop 1964). For example, it is interesting that physicians of his day and for many generations afterwards ridiculed his immediate cold water treatment for burns. We now know he was absolutely correct. He also clearly recognised the nature of scabies or itch (Stewart 1969), and his treatment of vomiting and diarrhoea with warm lemonade, a treatment to replace the electrolytes (sodium, potassium and citrates), is unsurpassed even by today's standards. On the other hand, there was also some attention given to magical treatments of the day e.g. fevers

treated with pills of cobwebs, cramps treated with a roll of brimstone under the pillow, a live puppy held on the abdomen for intestinal obstruction (this treatment was borrowed from the great Dr. Sydenham). To his credit, however, we must note that Wesley avoided most of the truly bizarre or dangerous or revolting treatments of his day, e.g. he permitted bleeding the patient for few conditions and deplored the almost universal use of this malignant remedy by physicians and, although he recommended the use of metallic mercury for certain conditions, he agreed that it was dangerous (Stewart 1969). Wesley had a wonderful way of dealing with those who presented a multiplicity of complaints. "Use the cold bath - this has cured many. This cured Mrs Bates of Leicestershire of the cancer in her breast, a consumption, a sciatica and rheumatism which she had nearly twenty years. She bathed every day for a month and drank only water" (Wesley Hill 1958). Electricity is also recommended as a cure for over twenty illnesses in *Primitive Physick*. It was one of his favourite remedies and he describes it as "far superior to all the medicines I know". In the preface of the 1760 edition he spoke enthusiastically of electricity, '*certainly it comes the nearest an universal medicine of any yet known in the world*' (Wesley 1760). Historical or contemporary writers have given little attention to this statement and the full implications of these words have yet to be appreciated.

John Wesley directed his handbook on the practice of medicine to a wide audience; in so doing, he chose the vehicles of directness, simplicity, and pure practicality. Nevertheless, despite its obvious emphasis upon matters of the body - matters pertaining to preserving the lives of his fellow men - John Wesley could not keep his '*Primitive Physick*' entirely free from what was, for him, the most important area of concern: the soul of man. Therefore, the only single remedy in which he could place his absolute faith becomes, really, the essence of the piece. "Above all," he maintains, "add to the rest, for it is not labour lost, that old-fashioned medicine - prayer; and have faith in God, who

killeth and maketh alive, who bringeth down to the grave and bringeth up" (Wesley 1747). "For the love of God, by the perfect calm, serenity and tranquillity it gives the mind, becomes the most powerful of all the means toward health and long life" - (which make John Wesley one of the founders of psychosomatic medicine as well as Methodism - (Weinstein 1956)). Moreover, John Wesley's own prescription for life - his complete faith in the gospel - had as much to do with the spread of '*Primitive Physick*' throughout eighteenth century Britain and America as did all the remedies and suggestions imprinted upon its pages (Rogal 1978).

3.3.3 'The Desideratum' (1759):

Wesley from 1751 onwards had become very interested in the subject of electricity generally, and in relation to the treatment of disease in particular. Several reports from England, Scotland and Sweden claimed that various ailments had been helped, if not cured, by the application of electricity (Menzie's 1980). So, for example, the use of electrotherapy had been reported in 1751 for a palsy of the tongue at Edinburgh Royal Infirmary and for other cases at Shrewsbury Hospital in 1754 (Cule 1982). It may be noted in passing that Franklin, Schaefer in 1752, Rossler in 1768 and Henley in 1779 were using electricity in treatment at about this time, and The Middlesex Hospital was the first hospital in London in 1767 to install a static machine (Baragar 1928). In 1747 John Wesley went "with two or three friends to see what are called the electrical experiments" (Wesley 1909). Wesley's Journal tells of various people helped by the electrifying process and of the way he conducted such experiments from 1753 thereon (Wesley 1909:4; 5; 6;). In March 1753, Wesley had been reading Benjamin Franklin's '*Experiments and Observations on Electricity*' and had concluded an entry in his journal with the exclamation: "What an amazing scene is here opened for after-ages to improve upon!" (Andrews 1969). In November 1756, he obtained an electrical

apparatus and arranged for the treatment of those “who were ill of various disorders and who might like to try a surprising machine” (Wilder 1978). He then proceeded at Southwark, the Foundry in Upper Moorfields, St Paul’s and at Seven Dials to electrify those suffering from a variety of illnesses. It is difficult to conjecture about the number of persons Wesley ‘electrify’d’ (to use his term). If the well-worn machine at City Road is any indication, there must have been many ailing souls knocking at his door who came daily in search of a cure (Rousseau 1968).

In 1758 Wesley had published another medical book, entitled *‘Advices with respect to Health Extracted from a late Author’* - a book of 218 pages. This book is especially interesting as it contains the first reference to electrical treatment to be found in any of Wesley’s works. He makes the claim that “electrifying cures all sorts of sprains”. There seems little doubt that Wesley derived his information in regard to electrical treatments from the works of Richard Lovett, a lay clerk at Worcester Cathedral. Lovett’s first book on this subject, entitled: *‘The Subtle Medium: or, that Wonderful Power of Nature showing its various uses in the animal economy, particularly when applied to maladies and disorders of the human body,’* was published in Worcester, in 1756. Lovett treated a large number of diseases by electricity, including St. Anthony’s Fire, bronchocele, contractions, epilepsy, feet violently disordered, gout, headache, mortification, palsy, rheumatism, sciatica, sore throat, and fistula lachrymalis and hysteria (Turrell 1921).

After spending several years overseeing the electrification of the London infirm (Methodists or otherwise), Wesley’s next step, quite naturally, focused upon publicising the ‘cure’ to a wider audience, particularly to those of his flock residing outside London. Thus on 31 October and 1 November 1759, the Methodist leader, in London, prepared his “Treatise on Electricity”. This was published in the following year as *‘The Desideratum: Or, Electricity made plain and useful. By a*

Lover of Mankind, and of Common Sense.' Five editions appeared during Wesley's lifetime, although, generally, the natural philosophers and the physicians of the period seem to have overlooked its existence (Rogal 1989) with the exception of Joseph Priestley (1767) who praised it in his classic '*History and Present State of Electricity, with Original Experiments*' (Haas 1994). The book was published anonymously. Possibly Wesley did this of set purpose, knowing the prejudice there was against him personally from many regular practitioners, and wishing to eliminate any cause that might make them continue in their neglect of a valuable means of treatment (Wesley Hill 1958). Nevertheless his interest in electrical matters was challenged in the 12th December 1760 *London Magazine*: "Why do you meddle with electricity". He replied, "for the same reason I published *Primitive Physick* [1747] - to do as much good as I can" (Haas 1994).

Wesley in 'The Desideratum' closely follows the practice of Lovett, to whom he frequently refers, and it may be fairly claimed that their two books set forth the sum of the theoretical and practical knowledge of that day about medical electricity (Wesley Hill 1958). The most remarkable feature of his own book, however, is the fervour with which he appeals for a trial of the curative effects of electricity (Turrell 1921). Even though he was often willing to speculate about causes of particular phenomenon he never sought to devise his own experiments to gain this understanding (Haas 1994).

3.3.3.1 A review and evaluation of 'The Desideratum';

The study of electricity was, in the 18th century, a most popular combination of amateur science and parlour magic. After reading Franklin's letters on electricity, Wesley came to feel that the subject was important enough to impress on his followers as '*The Desideratum*'. Written in two sections - the first telling of experiments and theories and the second discussing the application of electricity to medi-

cine - it is an admirable account of what was known about the subject up to the time of the publication (Schofield 1953).

The purest and least religiously motivated form of Wesley's empiricism is to be found in his preface to 'The Desideratum' in which, as Wesley puts it, "I have endeavoured to comprise the sum of what has been hitherto published on this curious and important subject, by Mr Franklin, Dr Hoadley, Mr Wilson, Watson, Lovett, Freke, Martin, Watkins, and in the Monthly Magazines" (Wesley 1759). This preface, it is true, evinces both a marked faith in electricity as a panacea and a firm grasp of empirical principles (Brantley 1984). All the important facts about electricity are now succinctly and ably presented with extracts from the published experiments and observations of these eighteenth-century workers. After these extracts comes the therapeutic applications of electricity, and Wesley gives a list of thirty-seven 'disorders in which it has been of unquestionable use.' He observes that 'a great part of these are of the nervous kind and perhaps there is no nervous distemper whatever which would not yield to a steady use of this remedy. It seems, therefore, to be the Grand Desideratum in Physic, from which we may expect relief when all other relief fails (Wesley Hill 1958).

3.3.3.2 Electricity made plain:

Citing Richard Lovett, Wesley wends his rhetorical way through ten prefatory paragraphs of generalized testimonials regarding electrifying, and concludes with the formers opinion that "the electrical method of treating disorders cannot be expected to arrive at any considerable degree of perfection, till administered and applied by the gentlemen of the faculty" (Wesley 1759). Such a moment in the history of medicine will never arrive, according to Wesley, until "the gentlemen of the faculty have more regard to the interests of their neighbours than their own; at least, not until there are no Apothecaries in the

land, or till Physicians are independent of them" (Wesley 1759). In the end the Methodist leader wishes only to encourage those who can relieve the suffering of poor and sick neighbours, hoping that '*The Desideratum*' will enlighten others who have little time and even less money to devote to the formal study of the issue (Rogal 1989). '*The Desideratum*' was not, of course, an original work as such; like so many books of that encyclopaedic age, it was a compendium of what was already known (Andrews 1969). However, the treatise claimed to be firmly based on experimental evidence; although Wesley does not recount any electrical experiments of his own, he reproduces accounts of more than a dozen experiments carried out by others (Andrews 1969).

John Wesley conducted his enquiries into electricity with characteristically thorough and painstaking research. The first part '*The Desideratum*' is concerned with setting out in forty-two numbered paragraphs all the information that he had been able to gather together. His own comprehensive and intriguing survey concludes with this: "To throw all the Light I can on the Subject, I subjoin a few Extracts from several other Writers" (Wesley 1759) The whole of it makes quaint and rather naive reading today. Having investigated the nature of this 'elementary fire' as he called it, Wesley went on to describe the uses to which it may be put and in particular its healing properties. Wesley proceeds to specify "several Disorders wherein Electrification has been found eminently useful" (Wesley 1759). The list of disorders is of great interest. Forty-three specific ailments are mentioned. Among them are blindness, chlorosis, contraction of the limbs, gout,¹ sciatica, pain in the back, and in the stomach. We know that he found the treatment particularly efficacious in cases of melancholia and, what are sometimes loosely called today, nervous disorders. With his enthusiasm, Wesley cannot resist a timely word of caution: "In order

¹ In former days gout was a common diagnosis, a kind of diagnostic carpet-bag into which were thrown many undifferentiated illnesses, e.g. eczema, headache, migraine etc. (Wesley Hill 1958)

to prevent any ill Effect, these two Cautions should always be remembered, First, let not the Shock be too violent; rather let several small Shocks be given. Secondly, do not give a Shock to the whole Body, when only a particular part is affected. If it be given to the Part affected only, little Harm can follow even from a violent shock" (Wesley 1759).

3.3.3.3 Electricity made useful:

Wesley, as curious and eager as any man ever was to investigate what was new, showed his natural disposition as a 'physician' in conceiving the possibility of this new discovery being used in the business of healing (Wesley Hill 1958). Wesley's major concern with electricity was over the possible applications to medicine, and he devoted almost half of his book to citations of the 'disorders' it could cure and of cases where it had been proved to do so (Schofield 1953). Doubtless in a great number of cases his treatment, while it did no harm, did no good; but here, in these initial stages of this kind of treatment, an immense and important value lay in the effort made and in making known results of the trial-and-error technique (Wesley Hill 1958). He had gathered his proof from many sources, Mr. Lovett's name being frequently mentioned. Various cases are reported from Newcastle-on-Tyne, Uppsala and Stockholm, from London and Edinburgh. Wesley had spread his net wide. There are bruises and strains, deafness, fistulae, ear-ache and tooth-ache, and hysterical cases. For example: "Sarah Ellison, caught cold in lying-in which fix'd a sharp pain in her teeth and the side of her face. She used all manner of means to remove this for upwards of six years. Among many others she had, at several times, 3 teeth drawn and was fourteen times blistered, but without effect. In July 1754 she received six shocks through the head. The pain ceased immediately and return'd no more" (Wesley 1760).

Wesley in his enthusiasm may have optimistically over-rated many of his results, but the main thing is that he was out to do good and to use every proper means that came to hand to do it. Undoubtedly he did much by these means to relieve suffering and inspire new hope while he blazed this new trail. In this his negative as well as his positive results were of value in ascertaining 'in what manner it might be most effectually applied in any case wherein it was proper' (Wesley Hill 1958).

3.3.3.4 The regular practitioner's response:

Wesley's opponents in this method of treatment were many and they included scientists of learned societies like the Royal College of Physicians and the Royal Society of London, but he nevertheless persisted in his belief that electrical shocks could do no harm unless the voltage was immoderately strong (Rousseau 1968). However, Wesley would have liked the backing of the medical profession (Cule 1990), but it was not forthcoming. This was also an example of the singular obtuseness of the medical profession during the greater part of the eighteenth century. They were like men with blinkers on. Their minds were closed to new methods. They were so inadequate that amateurs were breaking in on their preserves and they did not like it (Wesley Hill 1958) - a situation which has not been uncommon in the last two decades of the twentieth-century. Wesley's fellow practitioners in the healing art - the physicians and their good friends the apothecaries - decried electricity as a healing agent. It was useless; it was dangerous. But Wesley was not to be turned aside by opposition and isolation. Such antagonism rather stirred him to more fervent endeavour (Wesley Hill 1958). "Who can wonder that many gentlemen of the faculty, as well as their good friends, the apothecaries, decry a medicine, so shockingly cheap and easy, as much as they do quicksilver and tar-water"? But he also added the following caveat: "the latest medicine must be given quickly, whilst it is still curing. Must not Electricity

then, whatever wonders it may now perform, expect to share the same fate"? (Wesley 1759). This statement is most interesting in itself, for it shows an early insight into the mechanism of the placebo effect of an intervention, a subject not readily acknowledged until the beginning of the nineteenth century, and not subject to investigation until the middle of the twentieth century (see Beecher 1955). However, as this study goes on to show, Wesley's concerns over the future fate of electricity as a mere 'placebo' were not confirmed even two and a half centuries later.

Men like Lovett and Wesley, moved by compassion and by concern for the sufferings of their fellows, were searching for any means by which they might alleviate them. The newly discovered electricity appeared to them amply to offer such a means, and they could understand neither hesitation on the part of the professionals nor their opposition when others used it. "Being fully persuaded," writes Lovett, "that so extraordinary a phenomenon was never discovered to us but to answer some very valuable end: and though I began experiments of this kind at all adventures and at the greatest random possible, yet I had the pleasure and happiness to succeed far beyond expectation". Why then the general discouragement and opposition to its use? Why the obloquy heaped upon them for using it and obtaining cures even when other methods had failed? (Wesley Hill 1958). However, *'The Desideratum'* was not Wesley's final word on electricity, and his journals and letters reveal that for the next three decades he continued to advance the treatment. For John Wesley, electrifying certainly represented a disciplined commitment to healing, a frugal remedy that would complement well other of his prescriptions (Rogal 1989). In a letter to one of his preachers, John Bredin, he declared on October 19th 1781: "I do not know of any remedy under heaven that is likely to do you so much good as the being constantly electrified. But it will not avail unless you persevere therein for some time" (Wesley (1931) Letters 8;60.86).

3.3.3.5 Basic principles and practice of electrotherapy in the 18th Century.

In the eighteenth century electricity was the novelty which was holding men's attention, and Wesley at once seizes it for illuminating religious teaching, as this new discovery did not disturb his religion in the least. His faith was grounded in a personal relation to God, and the various modes of God's operation through the agency of natural law did not affect that faith. In the face of new knowledge Wesley's views of that part of God's operations might have to undergo modifications, but the core of his religious life remained unchanged. Accordingly Wesley became an electricity enthusiast (Pellowe 1927), and in about the year 1750 John Wesley procured an apparatus for electrifying patients, this may still be seen in his museum in City Road, London.

Wesley's Electrical Machine - it is one of at least four known to have been in his possession - consists of a hollow glass cylinder (7.5in long by 4.5in in diameter) supported on two wooden uprights. Through it runs a metal bar to which a handle is attached, by means of which the cylinder can be freely rotated. A leather pad (to which is firmly attached a piece of black silk) is pressed against the cylinder. It is controlled, very simply, by a thumbscrew. On an attached platform (8in long by 5in wide) and mounted on a glass insulating column, is a metal arm with a thin rod (9.5in long) attached to it, at the end of which is a small metal ball 1in in diameter. The whole 'machine' is mounted on four glass insulating legs (4.5in in height). Presumably the patient caught hold of the ball and as the metal arm made contact with the rotating cylinder, got a shock - the intensity depending upon the vigour with which the handle was turned. Also on view is a Leyden



jar of the period, it being 6.5in in height and 4in in diameter. Treatment by this method of storing an accumulated charge was also used, but it is recorded that Wesley himself preferred the machine. Possibly the more vigorous and obvious method appealed to a man of his temperament (Woodward 1962).

John Wesley and Richard Lovett were pioneers, enthusiasts, and ready to apply the use of electricity on every possible occasion, often in the face of much opposition, and not unmingled with attempted ridicule on the part of the medical faculty. The fact that these two were the first English speaking electro-therapists is most worthy of emphatic historical record - more than it has received - when we think of it as the source of that broad and vigorous river that has since flowed with increasing volume for the healing of the nations (Wesley Hill 1958). Wesley's enthusiasm is shown in his praises of this new healing aid - 'a thousand medicines in one, especially for nervous disorders', 'the greatest medicine yet known to the world' (Wesley Hill 1958).

3.3.3.6 Eighteenth-century treatment for mental illness.

Originally priest and physician were one and served the same functions. When more came to be known about the body and its illnesses, a group of practitioners arose who concerned themselves only with the body, whilst all things pertaining to the mind or soul, the immaterial substance, remained the province of the priest. Being neither by aptitude nor training equipped to deal with mind, physicians naturally treated mental patients through their bodies as though they were suffering from physical disease, by whatever means were in general use at the time, whether vomiting, bleeding, issues, setons or starvation (Hunter 1956). This briefly was the psychiatric scene in the first half of the eighteenth century into which portable electric machines were later introduced. Here was a new ethereal principle that could be felt when passed into the body and seen when drawn off as sparks, which caused strange sensations, had the power of making muscles contract, and paralysed limbs move. It was hailed as a panac-

cea and tried on every kind of illness whether mental or physical, and excellent results were reported in all sorts of conditions. In 1767, the Middlesex Hospital became the first teaching hospital in London to buy an electrical machine and the first asylum to employ an electrical machine was in Leicester, where in 1788 a room was set aside for electrifying patients (Hunter 1956).

3.3.3.7 18th Century indications v 20th Century applications

In summary, the disorders in which electricity was according to Wesley of unquestionable use, are shown in Figure I below.

Figure I: Wesley's (1769) list of disorders treatable with electricity

Agues - (fevers-malaria)
St Anthony's Fire - (Erysipelas)
Blindness, even from a Gutta Serena
Bronchocele - (goitre)
Chlorosis - (iron-deficiency anaemia)
Coldness of the feet - (?Raynaud's syndrome)
Consumption - (tuberculosis)
Contractions of the limbs
Cramp
Deafness, Dropsy
Epilepsy
Feet Violently disorder'd
Felons - (Whitlows)
Fistula Lacrymalis
Fits, Ganglions, Gout, Gravel
Head-Ach - (headaches and migraines)
Hysterics
Inflammations

Kings Evil - (Scrofula - tuberculous neck glands)
Knots in flesh
Lameness, Leprosy
Mortification - (gangrene)
Pain in the Back, in the stomach
Palpitation of the Heart
Palsy, Pleurisy
Rheumatism
Ringworms (Ringworm)
Sciatica
Shingles
Sprain
Surfeit - (over-indulgence)
Swellings of all kinds
Throat-sore
Toe hurt
Tooth-ache
Wen - (sebaceous cysts)

“It will be readily observed, that a great Part of these are of the nervous Kind; and perhaps there is no nervous Distemper whatever, which would not yield to a steady Use of this Remedy. It seems therefore to be the grand *Desideratum* in Physic, from which we may expect Relief when all other Relief fails, even in many of the most painful and stubborn Disorders, to which the human Frame is liable” (Wesley 1759).

And how correct Wesley’s (1759) statement seems to be. For if we examine the following list of conditions (Figure II) which are treatable by electricity, especially in the form of electroacupuncture, as we enter the twenty-first century, we then find that many of the conditions listed are the same as Wesley’s, with the exception of infectious conditions, e.g. agues and consumption (tuberculosis) etc.

Figure II: List of Indications of disorders treatable today

Indications Today

- a. acne vulgaris, acutely painful conditions; anxiety states and panic attacks; alcohol addiction; amenorrhoea; anal fissure; analgesia during childbirth; angina pectoris; ankle joint pain; arthrosis of jaw joint; asthma-bronchial;**
- b. biliary colic and dyskinesia; bronchitis - chronic;**
- c. cardiac neurosis; cardiovascular disorders; cholangitis; collapse; conjunctivitis - chronic; constipation; coxarthrosis; coxarthrosis.**
- d. deafness; depression; diarrhoea; dizziness; drug addiction; Dupuytren's contraction; dysmenorrhea; dysphagia;**
- e. eczema; enuresis; epicondylitis; exhaustion states.**
- f. facial paralysis; fainting; fertility-male; frozen shoulder.**
- g. gastric and duodenal ulcer; gastritis; gastroenterological disorders; gonarthrosis; gynaecological disorders;**
- h. hand pain; headache; haemorrhoids; hemiparesis; herpes; hyperemesis gravidarum; hypertension; hypotension.**
- i. impotence; intercostal neuralgia; irritable bowel disease;**
- k. knee joint pain.**
- l. labyrinthitis; lactation deficiency; leg ulcers; locomotor disorders; lumbar pain.**
- m. musculo-skeletal disorders - all; mental disturbances and illnesses; Meniere's syndrome; migraine; motion sickness; ME; MS;**
- n. neurodermatitis; neurological disorders; nicotine addiction;**
- p. periarthritis humeroscapularis; peripheral blood supply disturbances; prostatitis; pruritis vulvae; post herpetic neuralgia.**
- r. renal colic; respiratory disorders; rheumatoid arthritis.**
- s. salpingitis; sciatica; sense organ disturbances; sexual disturbances; skin disorders; spondylosis-ankylosing; spondylosis - cervical; sinusitis - frontal and maxillary; stress management;**

t. tennis elbow; thorax trauma; tinnitus; torticollis, trigeminal neuralgia and other facial pains including TMJ.

u. urological disorders, symptoms and psychogenic problems;

w. wound healing deficiency; wrist pain/carpal tunnel syndrome.

(after Pomeranz and Stux 1989)

This late twentieth-century listing is even longer and more comprehensive than Wesley's (1759) list, and no doubt he would see in modern orthodox and alternative or complementary medical electrotherapeutic practices a complete vindication of his advocacy of 'electrification'.

3.3.4 Holistic Health Care:

It was Socrates who said: "The reason for the frequent failure of Greek doctors is their inadequate knowledge of the whole, the health of which is a necessary condition of that of the part" (Tournier 1957). So from ancient times and through to the present day, the basic understanding of holism requires that the patient is seen as a multidimensional being who, affected by circumstances on one dimension, can have the results of those circumstances appear on another level (Webbern 1996).

3.3.4.1 Holism: definitions and principles

Holistic medicine is a philosophical approach to the study of man in health and disease. The patient is not just someone with an illness but is a dynamic open ended system, which is intelligent, and constantly maintaining a homoeostatic and balanced environment. The system is an interface between the outer environment and the in-

ner spiritual realms. The principle of holistic medicine is to support the system in its attempts to heal itself. In this context, healing is not only the maintenance of function but also the removal of stress factors from the body/mind system (Blom 1995). This means that, for example, someone with unresolved stress on a mental level (e.g. poverty or unemployment), can show symptoms of that stress on not just an emotional but also a physical level. So, for treatment to be given to cure the physical symptom alone, without attempting to discover and address the cause, is denying the principles of holistic practice and thus the opportunity of curing that patient fully (Webbern 1996).

3.3.4.2 Wesley's contributions to holistic health care.

Wesley did not lack confidence in his beliefs and was able to give to large numbers of patients the assurances that they needed in relation to the simple "certain cures" of which he wrote, whilst developing a reasoned view of which orthodox remedies were harmful. The efficacy of such a simplistic, positive approach in improving the patient's well being is now well recognised. He felt the need for treating the whole person, body and soul, and was thus a proponent of holistic medicine, although in his cautious, critical approach to the current pharmacopoeia, he would not have recognised himself as an exponent of 'alternative medicine' (Cule 1990). The question of whether, or not, Wesley should be regarded as an orthodox medical practitioner or as an alternative medical practitioner will be discussed in some depth later. Nonetheless, Wesley in recognising that the best treatment is always selective, showed himself to be a thoughtful and safe prescriber within the boundaries of traditional medicine, bearing in mind that in the eighteenth century the new facts of medical science were not enough to provide a firm basis for therapy (Cule 1990). Whilst these observations may be true to some degree, Wesley was also innovative and utilised effective unconventional treatments such as natu-

ropathic treatments, electricity and prayer with considerable enthusiasm.

In keeping with its literal meaning Wesley viewed health as wholeness or 'well-working' and his reading of seventeenth and eighteenth century physicians greatly influenced his perspective on health. For Wesley, the healthy body was critical to the individual's emotional well-being. As he quoted on numerous occasions, a 'corruptible body presses down the soul' (Wesley 1831;6:219) and "in the present state of human existence, when one part of the body is disordered, the total person suffers". This view is also reminiscent of St Paul, "That there should be no schism in the body; but that the members should have the same care one for another. And whether one member suffer, all the members suffer with it; or one member be honoured, all the members rejoice with it" (1. Cor. 12:25-26). It may well be that John Wesley's 'Whole' view had a Biblical inspiration (Richardson 1996). In short the body must be kept finely tuned for the good of one's total being (Ott 1989). However, Wesley did not suggest that health of body and health of soul are one and the same, but he did write of a remarkable and mysterious correlation between the two (Ott 1980a). The mind-body issue was considered under the rubric of the union of the soul and body and it was not that he was indifferent on the question of the soul's union with the body. Rather, for Wesley, the union was a mystery (Ott 1980b, note 15). Three themes gleaned from the medical community of his day supporting John Wesley's concept of health as wholeness are examined in some detail by Ott (1991) and are in essence:

1. that the body machine must work as a unit, whose parts are closely related;
2. that disturbance is communicated throughout the whole by 'sympathy' for example the emotions of the mind are capable of bringing about changes in the body;

3. that it is vital to understand the ancient and natural means of promoting healing and health - *vis medicatrix naturae* - the healing power of nature.

Wesley's commitment to the natural was evident in his consistent stress upon the relation between sensible regimen and good health, within a theological framework which stressed that the individual could live out the biblical mandate to be a good steward of the 'exquisite machine', the body (Ott 1991).

I will move on now to consider Wesley's interest in the passions and their considerable influence on health, "more so than most people are aware" (Wesley 1831;14:316), and his view that until the passions or emotional concerns are brought under control, the use of medicine will be to no avail (Ott 1989). Experience seems to show that violent and sudden passions dispose to, or actually throw people into acute diseases, and that deep and lasting sorrows sometimes weaken a strong constitution and lay the foundations for bodily disorders which are not easily removed. It remains to Wesley's lasting credit that he stressed the inter-relationship of physical and psychic or emotional well-being (Ott 1989). By passions Wesley intended such feelings as love, joy, hatred, sorrow, desire, fear, hope, and "a whole train of other inward emotions". These emotions constitute a "spring of action" for the soul. The opposite, for example, of being 'low-spirited' is completeness, wholeness, being at peace with oneself. If there is no peace, then one's health is in jeopardy, and so as long as the soul and body are united, then the emotions are bound to have their influence on the body (Ott 1980). This emphasis is consistent throughout his writings. (Ott 1989). "A contemporary perspective is that people talk of an age when we are exempt from passion. But the absence of passion really means anticipated death. If the frown of anger is no more, then the smile of pleasure will have gone as well; if there is no more indignation, neither will there be forgiveness; if there is no more anxiety, there will be no more hope either" (Tournier 1972).

3.3.4.3 Wesley's holistic prescription

John Wesley consistently urged Methodists towards a life-style conducive to good health and towards a programme of preventative medicine and therapeutic interventions, or, for example, a life of physical activity (Ott 1991). Wesley viewed a sensible regimen as the divinely appointed pattern of health and wholeness, and considered health as wholeness could be realized and preserved through the appropriate practice of sensible regimen (or manner of living) and the faithful use of 'that old unfashionable medicine, prayer' (Ott 1989). "Since the love of God, as it is the sovereign remedy of all miseries, so in particular it effectually prevents all the bodily disorders, which the passions introduce, by keeping the passions themselves within bounds. By the unspeakable joy and perfect calm, serenity and tranquillity it gives the mind, it becomes the most powerful of all means of health and long life" (Wesley 1747). On a contemporary level, prayer is still an important intervention for many and is recommended by physicians who practice the 'medicine of the person', especially common prayer in the community of faith which constitutes the Church, and which can often have psychological effects very similar to those of a medical cure. "In it I can feel that release of new life which renews my entire being. I can discover my person, my true feelings which have been held back or repressed until then, my likes and dislikes, my aspirations and my true convictions" (Tournier 1957). "Prayer may be said to be the breath of our spiritual life. He that lives cannot possibly cease breathing" (Wesley 1961;I). A Christian prays always, at all times, and in all places, and 'with all sorts of prayer, public, private, mental, vocal (Wesley 1765: Eph.6.18), and with the four parts of all prayers: deprecation (pleading for forgiveness and mercy), petition (asking), intercession (praying for others) and thanksgiving. Prayer prepares and enables him who prays to receive God's blessings (Wesley 1961;I - and after Borgen 1988).

3.3.5 Discussion

Eighteenth-century medical knowledge was still medieval medical knowledge, and we know that in this era there were few doctors in England who had attended medical school. The most enlightened physicians of Wesley's time placed the *vis medicatrix naturae* centrally in their therapy, and used such methods as they thought would assist and not hinder her healing power. However, Wesley's view of health and disease was essentially theological, and he was not content to think purely in terms of nature's healing, but looked beyond to the author of nature, deeming him to be wholly desirous of the good of his creatures (Wesley Hill 1958). By and large contemporary medical men despised Wesley and his work. The Establishment contempt was doubtless due to the fact that Wesley was not properly qualified, made little or no charge for his services, and was hugely successful (Menzies 1980).

3.3.5.1 Wesley as a physician or as an holistic alternative medicine practitioner

Wesley lived in a time of much illness when rapacious medical frauds seemed to be the rule rather than the exception. He studied medicine, which was no great task in his age, and then happily withstood, perhaps even invited, the criticism of practitioners. He was as qualified as most of the physicians of his time, and more so than many of them (Stewart 1969). But was John Wesley really qualified to practice medicine? If we consider his own list of requirements, published in 1748, for the practice of medicine, then it is evident that he did not meet them all (Bardell 1979):

1. *"Seeing life and health are things of so great importance, it is without question highly expedient that physicians should have all possible advantages of learning and education".*

2. *"That trial should be made of them by competent judges before they practice publicly.*
3. *"That after such trial they should be authorized to practice by those who are empowered to convey the authority".*
4. *"And that while they are preserving the lives of others, they should have what is sufficient to sustain their own (Wesley 1931;II).*

Wesley, however, believed that he was qualified as he satisfied the first requirement, stating that "for six and twenty years I made anatomy and physic the diversion of my leisure hours; though I never properly studied them, unless for a few months when I was going to America where I imagined I might be of some service to those who had no regular physician among them" (Wesley 1931;II). Wesley Hill (1958) also suggested that "The title Physician may rightly be granted to John Wesley because of his medical knowledge and skill," and more recently Cule writes: "his only unorthodoxy was the lack of any medical qualification, but he avidly read the works of those who had" (Cule 1990).

What authority had Wesley to take upon himself the role of physician? He acted on his own authority. He felt within himself the power or ability to meet the needs presented to him in the absence of many regular medical men, and with the inability of the poor to afford medical treatment - treatment which was most often inadequate and useless if not actually dangerous (Wesley Hill 1958). Nonetheless it was Wesley's theology which was the greatest single factor in fashioning the physician in him. Behind all he did there lay a certain view of God, of a universe whose supreme values were spiritual. He sought to heal men and women because he believed that he was thus fulfilling a God-given mission (Bowmer 1959).

Dr Wesley Hill, a medical doctor, goes on to describe John Wesley as a great amateur physician. His immense, up to date medical

knowledge, his sound sense, practical skill and sense of vocation, his advanced teaching of hygiene and physiological methods of cure, his readiness to break new therapeutic ground, his downright denunciation of the senseless blood-letting so popular with his contemporaries, his stricture of meaningless polypharmacy, his castigation of those evil-smelling concoctions and medicaments derived from filthy sources - all this adds up to a considerable total, especially when it points straight along the path that medicine has since travelled (Wesley Hill 1958:32). These views seem quite acceptable in the light of mid twentieth-century knowledge. As we approach the twenty-first century, and in view of the recent developments in the acceptance and practice of alternative and complementary medicine, I would like to suggest a fresh interpretation in that we could more accurately describe John Wesley as a great holistic alternative or complementary medicine practitioner rather than an orthodox medical practitioner.

The BMA in 1986 used the term 'alternative' to describe medical systems that are based on beliefs about the nature and causation of disease which are at variance with or antagonistic to current orthodox knowledge (Bakx 1991). The report also uses the word 'alternative' to qualify the word *therapy*. Here, the latter is only regarded as 'alternative' if it is worthy of use as a complement to, or a substitute for, orthodox practices. Wesley's practice of theological medicine, including the use of prayer, was certainly at variance with the orthodox humoral theories of the day. His therapies were usually used as a substitute for rather than to complement the more toxic orthodox treatment in vogue at this time. In this respect the use of monopharmacy rather than polypharmacy, electrotherapy rather than bleeding and blistering, prayer rather than purging and puking was prescribed, and this more gentle approach was denigrated by the orthodox practitioners of his time. Interestingly, the last two decades of the twentieth-century have seen a patient-led return to these less toxic treatments, including electrotherapy in its many guises. This is now to be found in

conventional orthodox medical and physiotherapy techniques such as Transcutaneous Electrical Nerve Stimulation (TENS) and Interferential - electrical stimulation therapy - using several different currents, as well as in alternative and complementary techniques such as electro-acupuncture and Acupuncture-Like TENS (ALTENS) - a situation, that I am sure would have been warmly welcomed by John Wesley himself!

3.3.5.2 Holistic medicine:

John Wesley realized that peoples' minds affected their physical, as well as their spiritual, life. He taught that it was not fear of sickness or death, but the fear of just being human that was the most prevalent and destructive fear of all (Wilder 1978). He consistently urged the Methodists towards the sound practice of the six non-naturals but his emphasis on the relationship between the non-naturals and good health also mirrored a long-standing conviction of the orthodox medical community. Wesley, however, enveloped this commonly accepted opinion in a theological framework which stressed, among other points, that sensible regimen was the divinely appointed pattern for a life of health and wholeness (Ott 1980a).

In 1955 Wesley Hill had examined the question, was John Wesley a medical Methodist? Medical Methodism was a school of medicine founded around AD 60, and which claimed a method by which medicine was made easy to understand. However, perhaps the closest connection between Wesley and those early medical Methodists, lay in their common belief in the efficacy of the physical means of diet and exercise as a therapeutic regimen (Wesley Hill 1955).

Throughout his writings, Wesley developed the theme of health as wholeness, i.e., a well-working of the whole. Well-working was the hallmark of the original created order. Though tarnished by Adam's disobedience, mankind is still endowed with an "exquisitely wrought

machine", designed to function properly within the limits of mortality (Ott 1980b); in Wesley's mind, holiness, happiness and health moved closely together (Rack 1982).

Wesley appeared to have had very little use for contemporary orthodox medicine. He set up an empirical system that, if we judge by popularity alone, worked at least as well as its more orthodox rival (King 1958). '*Primitive Physick*' was his great contribution to the simplification of what he saw as the best and safest in current therapy (Cule 1990), for he was a practical individual who, in medicine, wished to remain on a very simple level. There are several features of prime interest that characterize Wesley's therapeutic approach. For one thing, we note his devotion to frugality with drugs, a feature that must have infuriated the gentlemen of the faculties of medicine at the universities, and perhaps also the apothecaries who made their living selling medications. Also notable is his strong tendency to pragmatism in therapeutics. He was obviously in favour of whatever worked, and he would cheerfully recommend certain treatments as being strictly tried and tested, often on himself. Another feature was that he obviously used the principle that almost any sort of intervention is therapeutic, provided it is harmless and the sufferer believes that it has a chance of helping. The very simplicity and straightforward practicality of his treatment was inherently effective in many cases. The faith of the patient in the therapy is of the greatest importance (Stewart 1969). But perhaps the most important single feature in Wesley's therapeutic approach was his unconscious utilization of a precept that he could not have known or defined, i.e. 'homoeostasis', a concept formulated by the physiologist W B Cannon in 1939.

Dr. Cannon states that there are mechanisms operating to keep certain physiological variables, such as concentrations of body fluids and electrolytes and temperatures and pressures, within limits consistent with the normal function of the organism (Stewart 1969). A

good medical therapy is one designed to supplement this natural mechanism, supporting and strengthening it, and never rendering it inoperative. Wesley seemed to have a feel for homoeostasis (Stewart 1969).

Wesley also felt that medicine should be freely available for all, irrespective of ability to pay, and that those dealing with the sick had to take the whole patient into account. Further, he emphasised the importance of a healthy, nonindulgent, temperate life-style. He seems to have been careful to treat chronic rather than acute cases and to refer complicated ones to a physician or apothecary engaged for his dispensary (Rack 1982).

3.3.5.3 Empiricism

As Wesley assessed the matter, the trend of eighteenth-century medical care was away from the experimental or empiric approach to a rational or theoretical discipline. Consequently, "simple medicines were more and more disregarded and disused, till in a course of years, the greater part of them were forgotten". In place of simple remedies, physicians introduced an abundance of compound medicines consisting of so many ingredients, that it was scarce possible for common people to know which it was that wrought the cure. Such a practice of compounding medicines, Wesley argued, can never be reconciled to commonsense. Experience shows that one thing will cure most disorders, at least as well as twenty put together. As for the tendency to compound medicines, it can be "only to swell the apothecary's bill. Nay," Wesley added, "possibly on purpose to prolong the distemper, that the doctor and the apothecary may divide the spoil" (Ott 1980b). Judging by his discussion of approaches to medicine he regarded himself as a good 'empiric', following methods of trial and observation rather than tortuous classical theories of disease (Rack 1982). Choice of treatment for a disease had perforce to remain empirical until the

cause of that disease was known, when a remedy appropriate to it could be applied. Of course empiricism of itself is comforting. Whilst it relies on experience, it is supported by faith and dogma and is perpetuated by the mystery and power of the medical practitioner (Cule 1982:328). However, one may leave the ultimate comment to Wesley as he dryly remarked that “those who understood only how to restore the sick to health, they branded with the ignominious name of empirics” (Wesley 1747).

3.3.5.4 Electrotherapy:

Though unqualified practitioners, both Wesley and Lovett had a very real and genuine belief in the efficacy of electrical treatment, and their enthusiasm did a great deal for the early development of a science of which they were the first known practitioners in this country. Moreover, their work and their writings survived them for many years, and were frequently quoted by their qualified successors. Priestley in his book *‘The History of Electricity’* credits their work and concludes that “if in such unskilful hands it produced so much good, and so little harm, how much good, and how much less harm would it possibly have produced in more skilful hands!” (Turrell 1921). “What an amazing scene is here opened for after-ages to improve upon!” (Wesley 1909), and how well this statement fits in with Wesley’s life work too. These words were the prophecy of the wondrous increase in knowledge and practical application of electricity that has come about since these simple beginnings were made in the use of electricity in the healing art. The fulfilment of this prophecy is seen in the host of subtle diagnostic devices and the wide range of curative procedures available as aids to the modern physician (Wesley Hill 1958), and how much more so in the late 1990s. Wesley, by early 1753, had formed a clear thesis from which to consider and then confront the subject of electricity and the process of electrification. Wesley approached the project with characteristic order and thoroughness, but Rogal sug-

gests that he can hardly be identified as a pioneer in the administration of electricity for medicinal reasons. He carried forth the project more because of his faith in the phenomenon rather than his substantive knowledge of the healing arts; the Methodist leader attempted to compensate for his lack of knowledge and training by depending upon the work and the publications of more experienced predecessors and contemporaries who had practised healing the sick and the lame with various forms of electrical treatment (Rogal 1989).

Whilst these statements may be true to some degree it cannot detract from the great contribution that Wesley made to the practice of electrotherapy in the eighteenth, nineteenth and twentieth centuries and, dare I suggest, that of the twenty-first century too. His famous electric shock treatment can be cited as evidence of modernity, though in the eyes of a modern theologian it was used more like a quack's panacea (Rack 1982). Again I would argue that there is evidence that Wesley's electrotherapy was far in advance of his time by at least two and a half centuries! One only has to compare the two charts given earlier comparing the therapeutic application of the eighteenth-century with the twentieth-century to find a common theme. Had he just been a charlatan then he would have advocated electrical treatment for every kind of illness. Whereas the main applications for both eighteenth-century and twentieth-century practitioners would appear to be for musculoskeletal, neurological and psychological problems, and I have no reason to doubt that this will continue through into the twenty-first century.

3.3.5.5 Implications for 20th and 21st Century research and practice:

The medical historian, like the physician, must seek out those past events, connections, meanings, and background which enter significantly into the present, as parts of its living fabric (King 1958). The

divine influence of John Wesley lives on to the present day not only through the millions of members of the Methodist Church but also through his major contributions to holistic health care and preventative medicine. The implications of this work for the twenty-first century will now be considered.

Whether we should regard John Wesley as a 'quack' or accept him as an orthodox practitioner may be an open question, but what we cannot do is to ignore his safe and holistic approaches to eighteenth-century medical therapeutics in the form of simple medicines, naturopathic techniques, health prevention and electrotherapeutic procedures. Moreover, his approach anticipates a trend that is once again to be seen in evidence in the Western world. His stated interest in the experimental approach is also worthy of note, albeit bearing little resemblance to contemporary research, but he would surely welcome and endorse the world's current research programme into health care and not least in electrotherapy.

Wesley's holistic practice of medicine may also be seen as a template for contemporary orthodox and unorthodox practitioners. It is far too easy for both members of the orthodox medical professions and for alternative and complementary practitioners to pay lip-service to their 'holistic practices', but how many of we self-styled holistic practitioners really minister to the physical, psychological, social, environmental and spiritual dimensions of our patients? More significantly, how many of us really minister to the spiritual needs of our patients at all? Furthermore, how many of us are really qualified or able to do so? This aspect of care must surely be explored in the near future if we are to emulate Wesley's example of spiritual care, and whatever the choice of one's God. "What is your God?, Your mother, your own self-interest, your instincts, your pleasure, reason, science, or Jesus Christ?" (Tournier 1957).

How should we appraise John Wesley's enthusiasm for electricity as this new healing aid? - 'as a thousand medicines in one, especially for nervous disorders', 'the greatest medicine yet known to the world' (Wesley Hill 1958). I believe these statements still hold as true today as they did two and a half centuries ago, but so far we have not been able to prove him to be indubitably correct. There are hundreds of research papers examining the healing and pain-relieving properties of electricity, some of which are positive and some negative, but do we need more research to demonstrate that he was correct? No; I believe we have more than enough research to work on, but we do need to examine the evidence we already have, evidence that has not yet been subject to tertiary research in the manner of a systematic review and meta-analysis. To this end, the main thrust of the second stage of this thesis (Section 4) is my attempt to correct this deficit, by taking one example of electrotherapy, as applied to one area of health care, and then submitting it to a systematic review in order to produce a statement of efficacy. The therapy I have chosen is TENS (Transcutaneous Electrical Nerve Stimulation) as applied to chronic low-back pain. However, this will be the first and also the beginning of a whole series of systematic reviews of electrotherapy by others, as applied to the many conditions of health care which have already been well researched at this time, but which have failed to provide a definitive statement of efficacy for practitioners to utilise in practice.

3.3.6 Conclusion

The historian of science has an obligation to study not only the work of scientists in his period, but also the effects on science of any major social changes of that period. This obligation is particularly pressing in the case of 18th Century England since here, at that time, began the movement which led middle - and working-class Englishmen to a position of increasing importance in the political, economic, and eventually the scientific life of their communities. What these

people thought became important, and John Wesley, who helped form their thoughts and was, for many, their leader and spokesman, became important along with them (Schofield 1953). John Wesley, as a theologian and itinerant preacher, exerted a tremendous influence on the spiritual well-being of his audience; as a writer of a domestic remedy book, he exerted almost as tremendous an influence on the medical care provided in the home in England and in America (Baradell 1979). John Wesley's business was of course the saving of souls; but there was the important sideline of saving bodies too. Among the Methodist poor there were many chronically sick and unable to afford a doctor. Could something be done for them? (Ayling 1978). The answer was of course 'yes!'. This study has examined John Wesley's contribution to holistic health care, with a special emphasis on his electrotherapy techniques, followed by a consideration of the relevance and implications of his work both for the present and for the future.

The main aim of this study has been to present a fresh interpretation of John Wesley's eighteenth-century whole person healing ministry, in the light of the rapid development of holistic and alternative and complementary medicine in the last decade of the twentieth century. I have also set out to demonstrate the relevance of John Wesley's life and work for all interested parties, but especially for those interested in the current and future practice and research of holistic medicine, electrotherapy, and alternative and complementary medicine in the twenty-first century. However, in order to keep this study in balance I would like to end with the following caveat - "we know so much of him from his massive writing that generalization becomes inane and details confusing and one must be careful not to see in John Wesley just what one wants to see" (Stewart 1969). I trust I have not fallen too far into this trap!

Moving on from this history of medicine case study, with its implications for contemporary research and practice, and bearing in mind the ongoing developments throughout the 18th, 19th and 20th Centuries described earlier (3.2), the next stage of this historical and experimental review is to evaluate the basic mechanisms of pain, from a conventional western viewpoint, and to establish the accepted electrical parameters of electro-analgesia from the available published literature. This is necessary at this stage of the research in order to establish the conventional scientific bases of electroanalgesia in preparation for conducting the clinical research project and also to strengthen the foundations for the Ph.D. stage of tertiary research as systematic review and meta-analysis. The following sections (3.4 and 3.5) are dedicated to this evaluation.

3.4 Mechanisms of Pain

This section continues to build up the information background of this study with an examination of the current conventional physiological literature, relating to both the mechanisms of pain and to the principles and practice of electrical pain relief, in order that the following experimental stages of this thesis are based on the most up to date evidence available at the time of writing. This discussion is centred on conventional Western approaches, whilst the author recognises the existence of other paradigms especially those of Eastern origins, but these are not considered in this text.

Pain is one of the commonest symptoms in medicine and is said to be the prime cause of one third of all first consultations. While cure of the causative condition usually relieves the pain, it may on the other hand continue beyond its diagnostic usefulness, either because the disease is itself incurable, or because irreversible anatomical changes lead to continuing noxious stimulation (Bowsher 1987). Acute and chronic pain control is now a major concern especially with population ageing and associated pain of the chronic degenerative conditions of the elderly such as osteoarthritis, post-herpetic neuralgias, trigeminal neuralgia, reflex sympathetic dystrophy, 'thalamic pain syndrome' and malignant diseases. Thus in an ageing population the medical, social, and economic consequences of chronic pain may be expected to increase (Bowsher 1987).

3.4.1 Mechanisms of pain

The purpose of this brief review of the mechanisms of pain is to provide a certain amount of current insight into its complexities, and to serve as a basis for the discussion of the various physiological mechanisms surrounding the three main techniques of electroanalgesia discussed later in this section.

3.4.2 Pain and thresholds

Pain is not a simple, straightforward sensory experience, in the manner of, for example, seeing or hearing, as it has both emotional and physical components (Baldry 1993). The definition of pain recommended by the International Association for the Study of Pain is that it is an unpleasant sensory and emotional experience associated with actual or potential tissue damage (Merskey 1979). For a given noxious stimulus the intensity with which pain is felt varies from person to person, and with regard to this a distinction has to be made between an individual's pain threshold and pain tolerance (Baldry 1993). The pain threshold, like other sensory thresholds, is fairly constant, but pain tolerance level defined as the amount of pain a subject is prepared to put up with, varies enormously and clinically patients do not usually seek medical advice until they are beyond pain tolerance level, that is the degree of pain within which an individual can usefully be measured by using a visual analogue pain scale (Bowsher 1987). There are, however, several methods used to measure pain including the McGill Pain Questionnaire - a verbal selection method; the Submaximal Effort Tourniquet Test - a comparative physical test method; the Visual Analogue Scale - a progressive method using a 10cm line anchored by 2 extremes of pain; the 101-point Numerical Rating Scale (NRS-101) - a progressive numerical scaling method from 1-100; and several behavioural and verbal rating scales. A recent comparison of methods of measuring clinical pain intensity favoured the NRS-101 numerical rating scale as the most practical index, to the degree that a standard measure of pain intensity is needed to facilitate comparisons of treatment outcome, and to index chronic patient's pain intensity levels at different times in their lives (Jensen 1986).

3.4.3 Types of pain

Pain is occasionally purely psychogenic, though this is somewhat rare, but more often (when seen from a western neurophysiologi-

cal viewpoint) it is an organic physio-emotional experience occurring either as a result of the primary activation of visceral or somatic nociceptors, by disease or trauma or from potentially damaging stimuli, (nocigenic or nociceptive pain), or as a result of actual damage to the peripheral or central nervous system (neurogenic or neuropathic pain) (Baldry 1993). Referred pain is pain felt in a site or zone some distance from the primary site. There is much evidence to support several explanatory mechanisms for this phenomenon, and there are variations by case too, but it remains unclear which of these mechanisms are significant at this time. The structures identified, so far, in the complex processes of pain and pain relief include the sensory receptors, their associated afferent nerve fibres, the dorsal horns, ascending and descending pathways, the reticular formation in the midbrain and medulla, the thalamus, the limbic system and the cerebral cortex (see figure III).

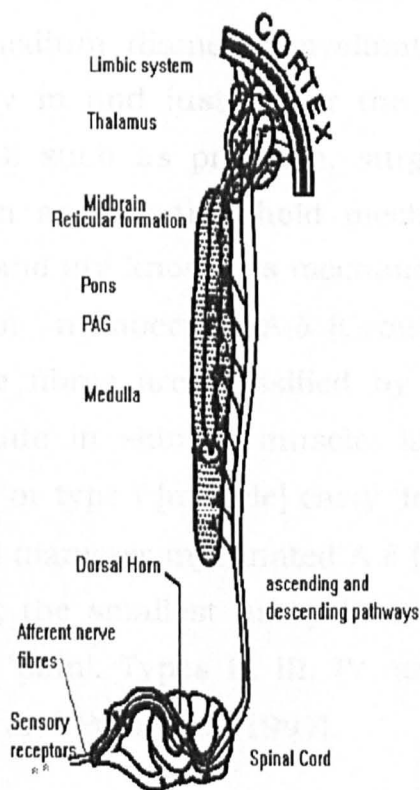


Figure III: The structures involved in pain and pain relief

3.4.4 Nocigenic pain, pain receptors, and their afferent nerve fibres.

Although the experience of nocigenic pain ultimately depends on interpretative processes in the neurons of the cerebral cortex, it occurs primarily as a result of a noxious stimulus activating myelinated and unmyelinated nociceptors (Baldry 1993). Two distinct types of receptor and peripheral nerve fibres subserve two distinct sensory experiences; A- δ nociceptors, with a multipunctate receptive field, transduce pricking or stabbing sensations (fast or first pain) which cause organisms to withdraw, whilst C-polymodal nociceptors, usually in a single receptive area, convey messages generated by tissue damage, (slow or second pain), which cause the organism to immobilise. The latter is morphine-sensitive; the former to all intents and purposes is not (Bowsheer 1987).

A- δ nociceptors: are connected to the spinal cord's dorsal horns via medium diameter myelinated A- δ nerve fibres, and are found mainly in and just under the skin. They are activated by noxious stimuli such as pressure, surgery, ischaemia, and sharps and are known as high-threshold mechanoreceptors. Some also respond to heat and are known as mechanothermal nociceptors. There are also a certain number of A- δ (Groups II and III) nerve fibres in muscle. (Nerve fibres are classified by size and according to whether they originate in skin or muscle: large diameter myelinated nerves A β [skin] or type I [muscle] carry 'touch' and proprioception, respectively. Small diameter myelinated A δ [skin] or types II and III [muscle] carry 'pain'; the smallest unmyelinated C [skin] and type IV [muscle] also carry 'pain'. Types II, III, IV, and C also carry nonpainful messages (Stux and Pomeranz 1991).

C-polymodal nociceptors: are connected to the spinal cord's dorsal horns via small diameter unmyelinated C afferent nerve fibres. They are called polymodal because of their ability to respond

to a mechanical, thermal or chemical stimulus. However, such activation is invariably only produced by chemicals released as a result of the ensuing tissue damage. The C nerve fibres connected to those present in muscle are called Group IV fibres. It is the stimulation of C-polymodal nociceptors in any deeply situated tissue such as muscle that leads to the development of slow onset pain, characterised by a widespread, ill-defined, deep seated and dull aching sensation. This activation is due to the effects of substances released and triggered by the damaged cells, which include bradykinin, histamine, leukotrienes, prostaglandins, platelet-activating factor and subsequently platelet serotonin, and substance P released from sensitised C-sensory afferents (Davis 1993).

The pain impulses, as afferent information, pass along the A- δ fibres and C fibres to the central nervous system. A- β mechanoreceptors are also present in the skin, muscles, tendons and joints and are not responsive to noxious stimuli but are activated by innocuous ones such as light touch and hair movement. A- β proprioceptors in muscle are present in the form of Type I muscle spindles, and in tendons as tendon organs. They are connected to the spinal cord's dorsal horn via large diameter A- β myelinated nerve fibres.

3.4.5 The Dorsal Horn and segmental mechanisms

The cells of the spinal cord are arranged in layers or laminae, six in the dorsal horn (I-VI), three in the ventral horn (VII-IX) and an additional column of cells clustered around the central canal as Lamina X (Baldry 1993 - Figures IV-V). The thin unmyelinated C nociceptive afferents terminate mainly in Laminae I and II where their axons secrete Substance P (SP) or (VIP) Vasoactive Intestinal Polypeptide, according to whether they arise from somatic structures or visceral ones respectively (Figure V). The medium size myelinated A- δ afferents terminate chiefly in Laminae I, II and V. The A- β afferents on entering the spinal cord, give off branches which make contact with

gamma-aminobutyric acid (GABA) mediated interneurons but most pass directly up the dorsal column to the medulla oblongata's gracile and cuneate nuclei. Axons from these nuclei form the medial lemniscus which terminates in the thalamus. The medial lemniscus is connected, via the anterior pretectal nucleus, to the periaqueductal grey area in the midbrain at the upper end of the opioid peptide mediated serotonergic descending inhibitory system (Baldry 1993). As a result of these connections, A-beta afferent activity is enabled to block the C afferent input to the spinal cord by promoting activity in this descending system (Bowsher 1991).

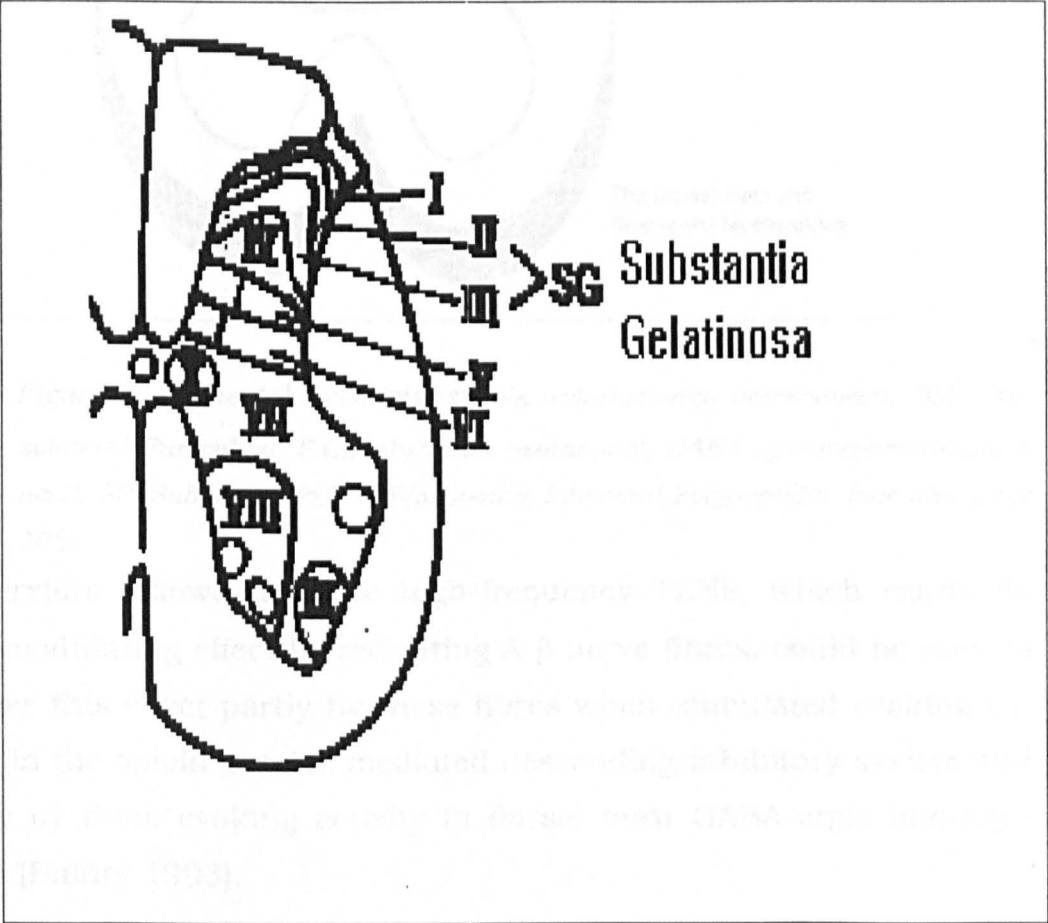


Figure IV: The Dorsal Horn

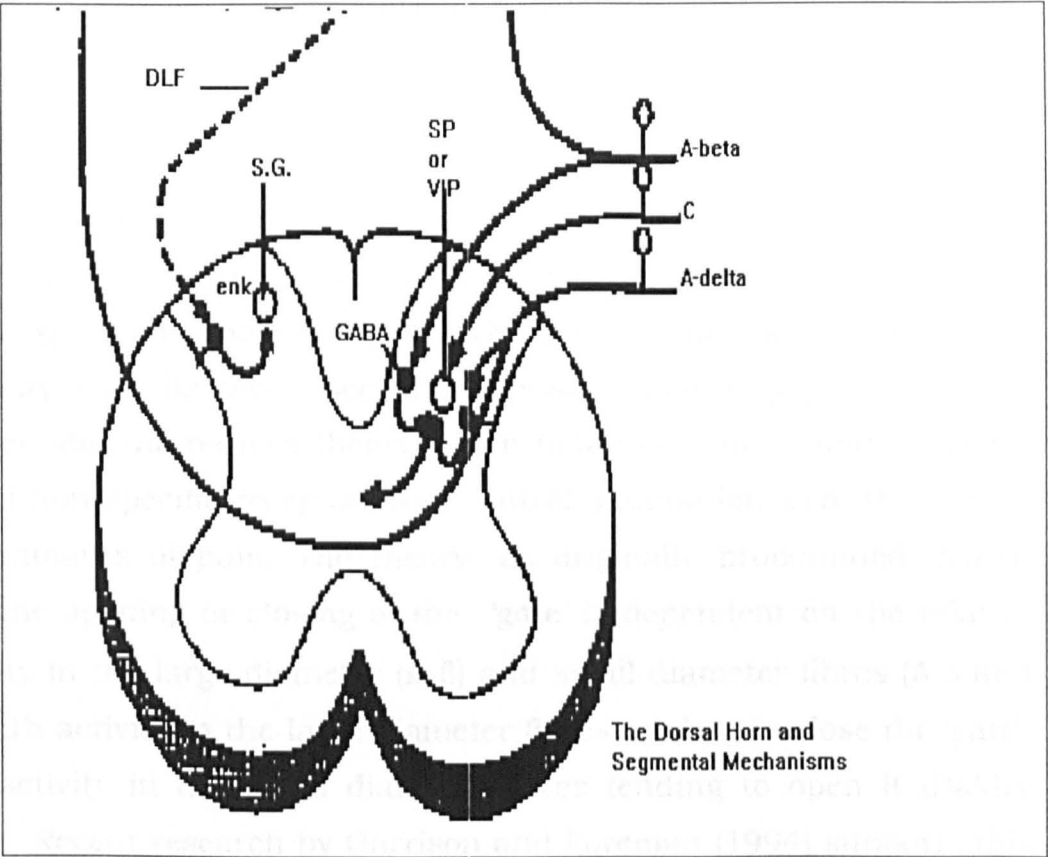


Figure V: Segmental mechanisms: ENK (enkephalinergic interneurons), DLF (Dorsolateral Funiculus), S.G.(substantia gelatinosa), GABA (gamma-aminobutyric acid), SP (Substance P), VIP (Vasoactive Intestinal Polypeptide). (see also page 105).

It therefore follows that the high-frequency TENS, which exerts its pain modulating effect by recruiting A- β nerve fibres, could be seen to achieve this effect partly by these fibres when stimulated evoking activity in the opioid peptide mediated descending inhibitory system and partly by them evoking activity in dorsal horn GABA-ergic interneurons (Baldry 1993).

There are three main types of dorsal horn transmission neurones - low-threshold mechanoreceptor cells, nociceptive-specific cells, and wide dynamic range cells which are responsible for transmitting sensory afferent information to the brain. The dorsal horn excitatory and inhibitory neurones modify the C afferent nociceptive information before reception and projection by the dorsal horn transmission cells.

3.4.6 The Gate Control Theory

Melzack and Wall (1965), developed their now-famous theory on pain mechanisms, which postulated that in each dorsal horn of the spinal cord there is a gate-like mechanism which inhibits or facilitates the flow of afferent impulses into the spinal cord before it evokes pain perception and response. Their theory was proposed as an alternative to the specificity theory of pain, which holds that pain is a specific modality with its own specialized sensors, neuronal pathways and centres and the pattern theory which maintains that stimulus intensity of non-specific receptors and central summation were the critical determinants of pain. The theory, as originally propounded, stated that the opening or closing of the 'gate' is dependent on the relative activity in the large diameter (A- β) and small diameter fibres (A- δ and C), with activity in the large diameter fibres tending to close the 'gate', and activity in the small diameter fibres tending to open it (Baldry 1993). Recent research by Garrison and Foreman (1994) supports this theory insofar as their study shows that dorsal horn neurons which can potentially transmit noxious information to supraspinal levels, can have their cell activity decreased during TENS application to somatic receptive fields. These findings are consistent with the concept of the 'gate control theory of pain' in that less noxious information would be involved in the pain perception process (Garrison and Foreman 1994). They also showed that there is a differential effect in that more cells respond to conventional high frequency, low intensity (TENS) variables than they do to low frequency, high intensity (ALTENS) variables. These results will also be considered again later.

The gate control theory proposes that the substantia gelatinosa, which caps the grey matter of the spinal horn in the spinal cord, is the essential site of control. The control mechanism is referred to as a 'gate' and is operated by external and internal influences. Pain impulses can only pass through when the gate is open, and not when it

is closed (Davis 1993). So if nociceptive input exceeds α - β fibre input, then the gate is open and the pain impulse ascends the spinal cord to the brain. If α - β fibre input exceeds nociceptive input then the gate is closed and the pain impulse is stopped or diminished due to the action of the inhibitory neurotransmitters and, therefore, does not pass up the spinal cord (Davis 1993). An essential part of the theory ever since the time it was first put forward is that the position of the 'gate' is in addition influenced by the brain's descending inhibitory system (Baldry 1993 - Figure VI).

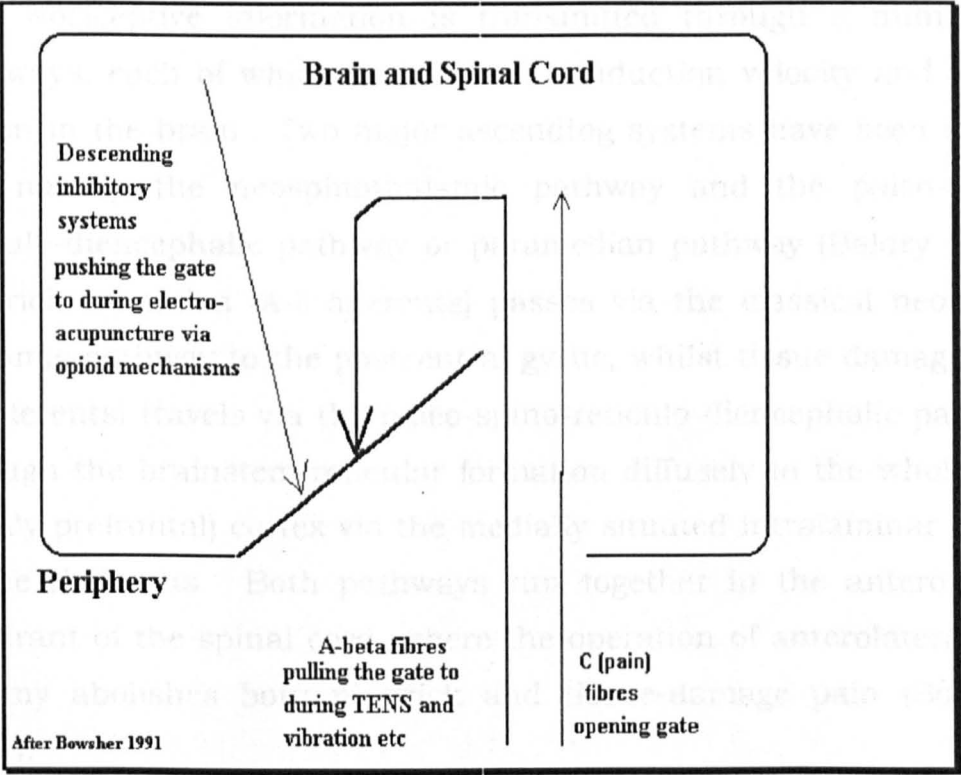


Figure VI: The Gate Control Theory of Melzack and Wall in relation to electroanalgesia as TENS and electroacupuncture

So entry into the central nervous system can be visualised as a gate, which is opened by pain-generated impulses and closed by low-intensity stimuli such as rubbing or mild electric stimulation (TENS), furthermore, it can also be closed by endogenous opioid mechanisms which can be activated from the brain or peripherally by acupuncture (Bowsher 1987) or by gentle rubbing, massage, electrical stimulation and hot or cold therapies. Comments and criticisms of the gate control theory are examined more fully in the discussion section (3.4.13).

3.4.7 Central pain pathways: ascending pathways (Figure VII)

Nociceptive information is transmitted through a number of pathways, each of which has its own conduction velocity and termination in the brain. Two major ascending systems have been identified namely the neospinothalamic pathway and the paleo-spino-reticulo-diencephalic pathway or paramedian pathway (Baldry 1993). Pinprick sensation (A- δ afferents) passes via the classical neospinothalamic pathway to the postcentral gyrus, whilst tissue damage pain (C afferents) travels via the paleo-spino-reticulo-diencephalic pathway through the brainstem reticular formation diffusely to the whole (but mainly prefrontal) cortex via the medially situated intralaminar nuclei of the thalamus. Both pathways run together in the anterolateral quadrant of the spinal cord, where the operation of anterolateral cordotomy abolishes both pinprick and tissue-damage pain (Bowsher 1987).

The reticular formation contains several nuclei, which make important contributions to the experience of pain, and the behavioural activities associated with this. One of these is the nucleus reticularis gigantocellularis which responds to noxious stimuli and contains serotonin cells, which, together with the nucleus raphe magnus and neurons in the periaqueductal grey area of the midbrain from which they receive an excitatory input, form the upper part of the opioid

peptide mediated descending inhibitory system that is of such importance in the control of pain (Baldry 1993).

The limbic system consists of a group of structures (hypothalamus, hippocampus, amygdala, and the cingulum bundle) clustered around the thalamus and evidence suggests that these structures control the motivational and behavioural responses to pain together with appropriate emotional responses.

The frontal cortex has a controlling influence on the nature of pain with cognitive activities such as memories of past experiences, mood and prevailing circumstances as well as the paramedian system's motivational-affective ones (Baldry 1993). The perception of pain does not simply involve a moment-to-moment analysis of afferent noxious input but involves a dynamic process, which is influenced by the effects of past experiences. Sensory stimuli, therefore, act on neural systems, which have already been modified, and the behavioural output is significantly influenced by the 'memory' of these prior events (Coderre 1993). It is also suggested from the evidence available that there are specific cellular and molecular changes that affect membrane excitability and induce new gene expression, thereby allowing for enhanced responses to future stimulation. Finally, anxiety is rarely considered as a cause of pain but persistent pain is commonly associated with the development of psychological problems including anxiety, muscle tension (and further pain) and depression.

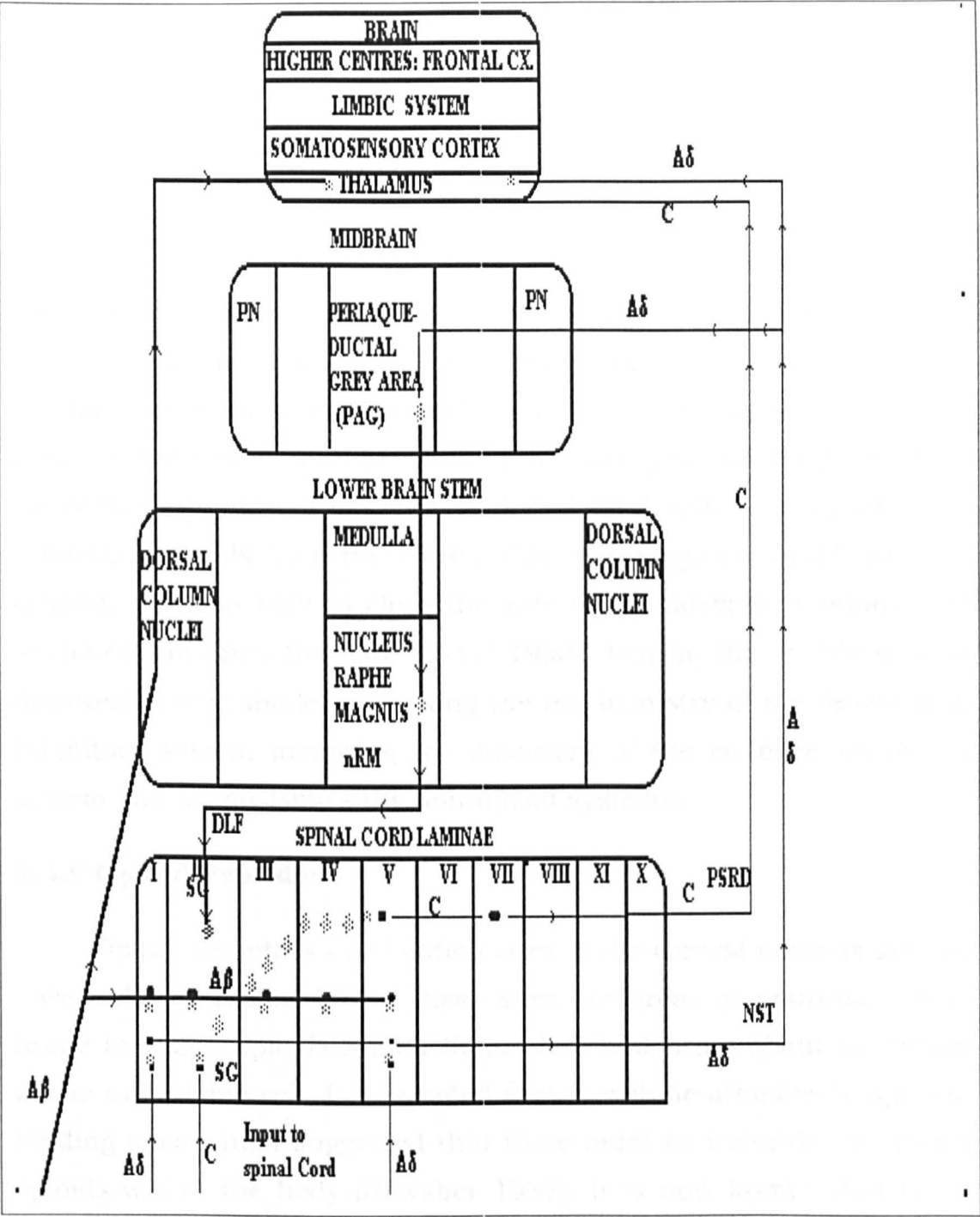


Figure VII: Diagrammatic representation of spinal cord dorsal horn nocigenic input and the two ascending 'pain' pathways - the neospinothalamic (NST) carrying A-delta 'pin-prick' information and the paleo-spino- reticulo-diencephalic pathway (PSRD) carrying C 'tissue damage' information. The descending inhibitory pathway - the dorso-lateral funiculus (DLF) is also shown linking the periaqueductal grey area (PAG) with the nucleus raphe magnus (nRM) and the dorsal horn substantia gelatinosa (SG).

3.4.8 Central pain pathways: descending pathways (Figure VII)

In 1954 Hagbarth and Kerr found that stimulation of either the reticular formation, the cerebellum, or the cerebral cortex has a controlling influence on the flow of nociceptive impulses up the anterolateral tract, and concluded that this must be because each of these structures is capable of exerting a descending inhibitory effect on dorsal horn transmission cells (Baldry 1993). Descending impulses from the brain stem and cerebral cortex and thalamus appear to have an effect on the spinal gating system by modifying the opening and closing of the gate via the descending dorsolateral spinal cord pathways. Inhibitory signals from the cortex, due to feelings of confidence and control, will also help to close the gate whilst adverse emotions and anxieties will open the gate (Davis 1993). During the 1970's several discoveries were made concerning the biochemistry of the descending inhibitory system including the discovery of the endogenous opioid system and in the 1980's the non-opioid systems.

3.4.9 Opioid Peptides

Opiate receptors - or binding sites in the central nervous system - were discovered in 1973. These sites are areas of neuronal membrane to which opioids attach themselves and bring about inhibition in the underlying cell. It was noted that morphine attaches to specific binding sites which suggested that there must be naturally-occurring opioids within the body (Bowsheer 1987). It is now known that there are four distinct types of opioid receptor, mu, kappa and delta and sigma. There is a widespread distribution of opiate receptors within the Central Nervous System. These are numerous in the paramedian system's intralaminar thalamic nuclei, reticular formation and limbic structures. There are only a few in the neospinothalamic system's ventrobasal thalamus and post-central gyrus. In the dorsal horn there are large numbers situated postsynaptically on neuronal membranes and there are some situated presynaptically on the intraspinal part of

C afferent nerve fibres (Baldry 1993). Thus opioid binding sites (receptors) occur at many synaptic and non synaptic sites in the CNS, notably the spino-reticular system, and inhibition results from the action of exogenous opioids (e.g. morphine) or endogenous opioids (e.g. enkephalins, endorphins) at these sites (Bowsher 1987).

Once the opiate receptors had been found then the search began for the endogenous opioids. The first to be identified were the enkephalins, isolated from pig brains by (Hughes 1975). After the discovery of the enkephalins - Leucine and Methionine, others soon followed including beta-endorphin, dynorphin in 1979 and decapeptide alpha-neoendorphin in 1981 - three distinct families of opioid peptides at the time of writing.

Studies of the distribution of endogenous opioid peptides have shown that there are high levels of enkephalins and dynorphins in the limbic structures, periaqueductal grey area, the nucleus raphe magnus and the substantia gelatinosa of the dorsal horn (with spill-over into the cerebrospinal fluid), and anterior pituitary and adrenal medulla, with release into the plasma. Plasma enkephalins are released from the adrenal gland, the gut, sympathetic ganglia and peripheral autonomic neurons (Baldry 1993).

The Dorsolateral funiculus is the descending serotonin (5-hydroxytryptamine; 5HT) inhibitory system which arises in the nucleus raphe magnus of the medulla and the periaqueductal grey (PAG) area of the midbrain and exerts its effect on neurons in the dorsal horn (Figure VII). This descending inhibitory system is brought into action either via collateral's which form a link between the neospinothalamic 'A- δ pin prick' ascending pathway with the PAG: or via collateral's which form a link between the PAG and the medial lemniscus, which arises from the dorsal column nuclei connected to A- β fibres in the dorsal column. The pain suppressing effect of anti-depressants is

probably due to their ability to enhance transmission down this pathway by blocking the uptake of 5HT (Thompson 1995).

3.4.10 Opioid peptide mediated descending inhibitory system

It is now known that there are several descending inhibitory systems but the one we know most about is the one mediated by opioid peptides. In this system, the midbrain's periaqueductal grey area has inputs from the thalamus and the hypothalamus. the amygdala, and the frontal cortex, projects to the medullary-situated nucleus raphe magnus and nucleus reticularis gigantocellularis. Serotonergic axons from these latter structures descend in the dorsolateral funiculus to end in synaptic contact with enkephalinergic interneurons situated on the border of Lamina I and II of the dorsal horn (Baldry 1993). The descending dorsolateral pathways effect is in part due to the release of endogenous opiate neuromodulators which close the gate by inhibiting the release of substance P and opioid serotonergic and non-opioid noradrenergic descending mechanisms which are capable of blocking upward transmission of pain generated impulses (Bowsher 1987). The spinal interneurons, when activated in this manner exert an inhibitory effect on the dorsal horn transmission cells responsible for projecting nociceptive information received from C-polymodal afferents upwards via the paramedian pathway (Baldry 1993).

Figure VIII shows the central nervous mechanisms of pain control: nociceptive tissue damage information reaches the substantia gelatinosa (SG) of the spinal cord via C afferent fibres. SG cells can be postsynaptically inhibited by enkephalinergic interneurons (ENK) which are activated either by A-delta pinprick fibres as they enter the spinal cord or via serotonergic (5-HT) inhibitory fibres that descend in the Dorsolateral Funiculus (DLF) from the nucleus Raphe Magnus (nRM) of the medulla oblongata. The nRM being activated from the periaqueductal grey matter (PAG) in the midbrain - the descending in-

hibitory system. Spinothalamic (ST) fibre collaterals can activate the PAG, arising from spinal cells excited by A-delta afferents, from higher centres and from the pretectal region in the midbrain. Collaterals from the medial lemniscus arising in the dorsal column nuclei excite the pretectal region; A-beta fibres travelling in the dorsal columns activate these in turn.

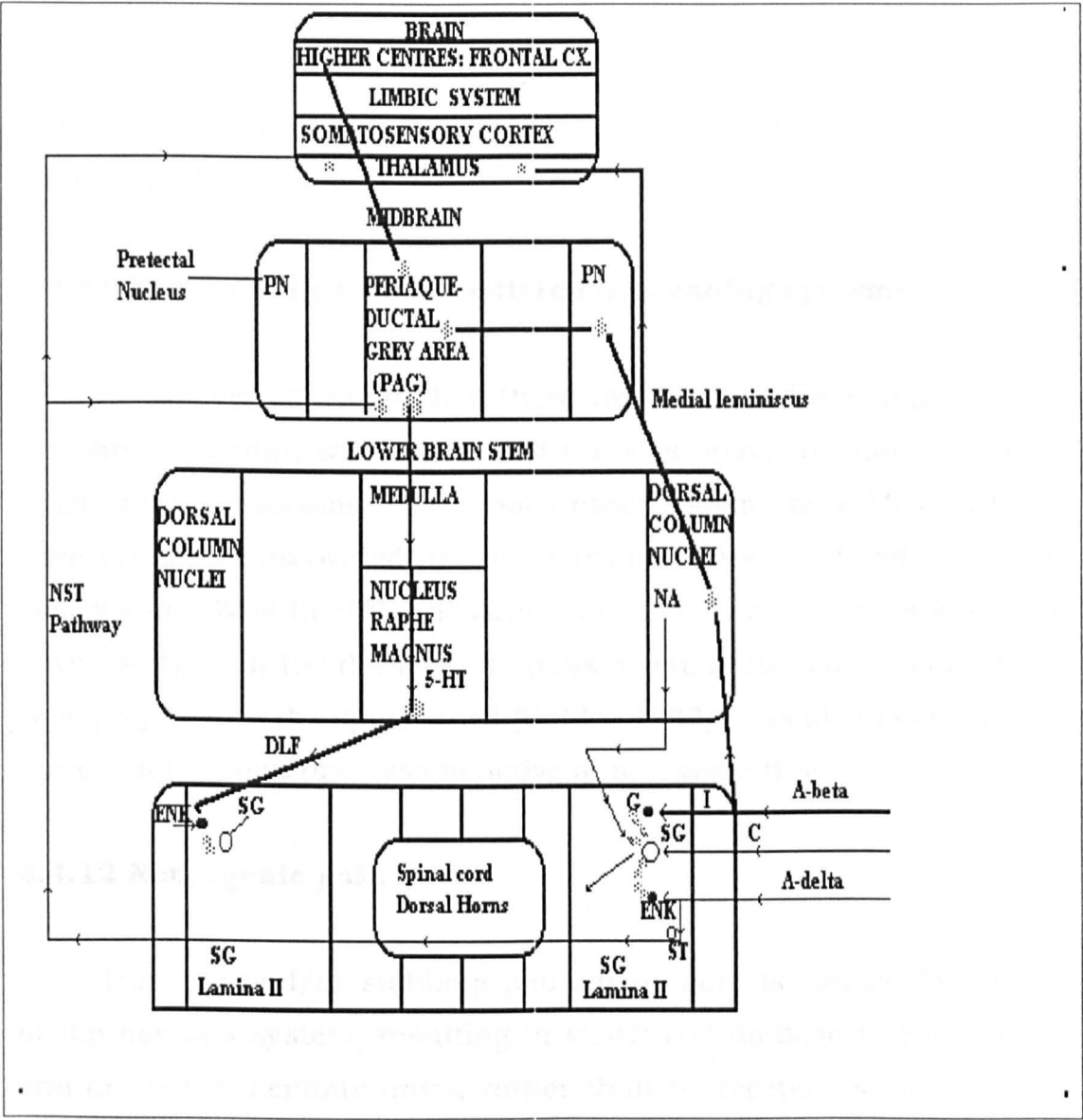


Figure VIII: Central nervous mechanisms of pain control

The A-beta, on entry to the dorsal horn, also excite inhibitory GABA-ergic interneurones (G) which presynaptically inhibit input to SG. Inhibitory noradrenergic fibres descend from the Locus Coeruleus

(NA) and other brain stem cell groups to exert direct inhibitory action on the Substantia Gelatinosa; this inhibition is not mediated via enkephalinergic or GABA-ergic interneurons (after Bowsher 1991).

This system can be activated spontaneously by frontal cortex activity or induced by exogenous stimulation of A- δ afferents setting up activity in the neo-spinothalamic ascending pathway, which at the midbrain level gives off a collateral to the periaqueductal grey area, or as a result of A- β nerve stimulation setting up activity in the dorsal column-medial lemniscus ascending pathway which also projects to the PAG (Baldry 1993).

3.4.11 Non-opioid peptide mediated descending systems.

It is now accepted that there are several descending control systems, and that, whereas one of these is opioid peptide mediated, others must be mediated by various other transmitters. Most of these have yet to be discovered and their transmitters identified. However, Melzack and Wall in 1988, describe one such system that is known to have its origin in the dorsolateral pons where noradrenalin-containing cells project into the spinal cord (Baldry 1993). It is also possible that there is more than one system active at any given time.

3.4.12 Neurogenic pain

Burning and/or stabbing neurogenic pain is caused by lesions of the nervous system, resulting in structural damage to the peripheral or central nervous units, rather than by receptor stimulation as described above. Neurogenic pain is much less responsive than nociceptive pain to the electroanalgesia techniques of evoking activity in endogenous opioid peptide and non-opioid peptide mediated pain modulating mechanisms. It is also mostly resistant to narcotic analgesics, as well as the endogenous opioid peptides, but can sometimes be

relieved by sympathetic blockade, tricyclics (which facilitate noradren-
ergic inhibition) and anticonvulsants (Bowsher 1987). However, some
elderly patients with neurogenic pain respond very well clinically to
electrical stimulation.

3.4.13 Discussion:

The gate-control theory has been extensively criticised in the
past, not least by Prof. Nathan (1976):

"The gate-control theory was worked out to explain certain facts that had been found from investigating the physiology of the region where afferent fibres deliver impulses into the posterior horns. The theory itself has been productive of further work in this territory. It was one way of explaining some of the facts that had been observed. But, as fortunately always happens, further physiological and histological investigations have shown that what happens here is more complicated than was first thought. The gate-control theory emphasised that pain is not an invariable result of small delta and non-myelinated nociceptive fibres, and - more important - that pain may result from the excitation of fibres that are not normally concerned with conducting impulses that finally cause pain. Ideas need to be fruitful; they do not have to be right. And, curiously enough, the two do not necessarily go together. Melzack (1973) wrote in 'The Puzzle of Pain' on the theories of the last hundred years as follows: ... each change contains a major conceptual idea that has a powerful impact on research and theory. The same must be said of the gate-control theory" (Nathan 1976).

So advances in knowledge since 1965 have led to the theory being revised several times, e.g. examining the role of the substantia gelatinosa; the effects of C fibre stimulation; location and mechanism

of the gate, however, despite continuing controversy over details the fundamental concept underlying the gate theory has survived in a modified and stronger state accommodating and harmonising with, rather than supplanting, specificity and pattern theories. It has also stimulated multidisciplinary activity, opened minds and benefited patients (Verrill 1990) and the more recent studies such as Garrison and Foreman (1994), described earlier, have also strengthened the underpinning of the gate control theory.

There are, however, several clinical observations on the control of pain, which are not in accord with the gate-control theory. Transcutaneous electrical nerve stimulation was developed on the strength of the theory for the control of chronic and post-operative pain using low-intensity, peripheral electrical stimulation applied locally within the dermatome as the pain. However, it has been recognised for centuries, especially within the Traditional Chinese Medicine literature, that pain can be controlled by stimulation at points distant to the pain e.g. with the use of acupuncture or electrical stimulation and this observation is at odds with the theory. It has been recently suggested that this stimulus has to be intense and has given rise to the theory of Diffuse Noxious Inhibitory Control (DNIC), in that a number of pain-relieving stimuli share some common characteristics: the painful or unpleasant nature of the stimulus; widespread analgesic effects; associated long standing post-effects; a requirement of ascending-descending pathways with presumably the 'analgesic system' as a link and final inhibitory effects upon convergent units. DNIC as described by LeBars (1979a/b) seems to offer the neuronal basis of such a phenomenon. Further clinical evidence for the existence of a pain inhibiting system of peripheral origin is the observation that organic pain raises pain thresholds in other areas of the body (see Hazouri and Mueller 1950 and Merskey and Evans 1975) and that an anterolateral cordotomy which relieved root pain in paraplegics produced a lowering of the pain thresholds in other body areas. Le Bars conclude with the

sition that DNIC may, on the one hand, explain certain paradoxical pain-relieving effects and on the other, allow, by means of a contrast system, a significant pain signalling message to emanate from the convergent neurones of the dorsal horn (LeBars 1979a/b and 1989). However, the inhibition remains after the noxious stimulus has been removed but only for a few minutes and thus leaves much to be desired as a clinical procedure. There are more contentious areas of pain control, which most definitely do not fit into the conventional paradigm i.e. of the gate-control model, endogenous opioid peptides model or the diffuse noxious inhibitory control model. For example, the use of auricular acupuncture and body acupuncture not carried out in the same dermatome as the pain, which is explained by an eastern paradigm relating to energy systems and releasing blockages. Moreover, any stimulus applied to acupuncture needles or surface electrodes does not necessarily have to be a noxious one to obtain satisfactory pain control, especially if electrical stimulation is employed, as the parameters of the electrical pulse, wave form and frequency, seem to be more important than intensity of stimulation and these areas are considered in more detail in the next section.

3.5 Mechanisms of Electrical Pain Relief.

This section examines the fundamentals of electrical pain relief methods in order to establish current accepted and recognised parameters of electro-stimulation and treatment as described in the literature. This is necessary because of the confusion, which often surrounds these aspects of electrostimulation, in order that the research studies to be presented later in this thesis are based on sound, and accepted clinical electrical treatments, which in turn are based on recognised and adequately researched electrical parameters.

3.5.1 Pain control by electrical methods

There have been two recent review papers examining both transcutaneous electrical nerve stimulation and electroacupuncture. The first deals with transcutaneous electrical stimulation, which was reintroduced into medical and complementary practice in the early 1970's. Since that time, numerous studies, both controlled and uncontrolled, have suggested its utility for the treatment of pain related to acute musculoskeletal injury, postoperative pain, pain of peripheral vascular origin, pain of myocardial ischaemia and chronic pain of a variety of causes. Pain of labour in delivery was affected equivocally. Pain complicating cancer has not been reliably relieved to date. A small number of controlled studies failed to demonstrate benefit, but the preponderance of evidence suggests that electrical stimulation of the peripheral nervous system is a useful adjunct in the management of many pain states. Most studies indicate that the resultant analgesia of TENS is not opioid-dependent. Pain threshold and perception both appear to be reduced. The physiological mechanism by which pain is affected is not defined in this paper; but local neural blockade, branch block in the dorsal horn and activation of a central inhibitory system have all been postulated (Long 1991).

The second review considered the serious basic research on electroacupuncture, which began in 1976 following the acupuncture endorphin hypothesis. There was an enormous amount of rigorous research into these mechanisms and these studies are comprehensively examined up to 1988 by Pomeranz and Stux (and other contributors), concluding with the observation that 'we now know more about acupuncture analgesia mechanisms than many conventional medical procedures' (Pomeranz and Stux 1989). This review has recently been updated and will be discussed in some detail in the following text (Stux and Pomeranz 1995).

3.5.2 Therapeutic Currents

Research in the 1980's by Prof. Jisheng Han, using a western approach rather than a Traditional Chinese Medicine Model, at Beijing Medical University in China, showed that electroacupuncture at 4pps (pulses per second) releases enkephalins while at 100pps dynorphins were released, he used antibodies to enkephalins injected intrathecally into the spinal cord of rats to block acupuncture analgesia produced by 4pps, with antibodies to dynorphins blocking 100 pps analgesia (Han 1989). Han concluded that low-frequency EAP depends on the release of Beta-endorphin in the brain and Met-enkephalin in the spinal cord, whereas high-frequency EAP analgesia is mediated by dynorphins in the spinal cord. Recent research by Richard Cheng in Toronto Canada has also shown that 4pps work through the endorphin mechanisms, while 200pps stimulation is mediated by the monoamines, serotonin, and norepinephrine (Cheng 1989). Some pulse generators use trains of pulses i.e. bursts instead of continuous pulses, with an internal frequency of say 200 pps and a repetition rate of 1 pps. In this way both endorphins at 1 pps and serotonin at 200 pps can be released. However to achieve De Qi, the dull aching sensation preferred by Traditional Acupuncturists, it is necessary to simulate strongly at 1-4 pps in continuous mode. This strong

to release cortisone and endorphins via activation of type III efferents. De Qi is a mild, pleasant, ache, which is easily tolerated by most patients. There is very little danger from this type of electrostimulation as the units are battery operated and use currents well below the levels which can affect the heart. However, patients with on demand pacemakers should not normally be treated and stimulation over the front neck region should be avoided to prevent laryngospasm (Stux and Pomeranz 1995).

3.5.3 Electrical Equipment

There are numerous electrostimulation units available today of variable design and efficacy. A biphasic generator is usually recommended for electroacupuncture and TENS, i.e. a negative pulse followed by a positive pulse or vice versa is generated by the unit, this reduces polarisation of each needle due to electrolysis. The negative pulse cleans the electrode of electrolytes deposited by the preceding positive pulse and if the pulses are perfectly biphasic (symmetrical biphasic pulses), then the net DC current is zero and no polarisation occurs. Polarisation raises the electrode resistance over time, thus reducing the intensity of stimulation, and creates a tendency for the needles to break off in the tissue (Stux and Pomeranz 1995). Since negative pulses cause an action potential on the nerve, it is important that both needles in a pair receive negative pulses, which is only possible in a biphasic stimulator (Stux and Pomeranz 1991). The intensity of stimulation is under the control of an intensity knob, and in order to achieve an optimum effect for acupuncture analgesia, the strongest tolerable intensity is required for De Qi to activate type II and III muscle nerves (Stux and Pomeranz 1995). To achieve De Qi from type III nerves usually requires stimulus intensities 5 to 10 times threshold levels for muscle contraction i.e. 25-50V, 2.5-5ma, at a pulse width of 0.1ms. The pulse width is usually variable between 0.1 and 1.0ms. Another critical parameter is the pulse frequency usually expressed as pps (pulses per second) or as Hertz or Hz. In ancient

China the needles were often manipulated with a rhythm of 2-4 pps (Stux and Pomeranz 1995).

3.5.4 Physiological Responses

In ancient times in order to stimulate the nerves the acupuncture needle was manipulated in and out to create 'De Qi', a deep aching sensation, with fullness, tingling, and numbness (Stux and Pomeranz 1991/95). Stimulation of high threshold muscle sensory nerves (type II and III efferents) appears to be the basis of acupuncture analgesia (AA). Neural messages are sent to the brain (or spinal cord) where neurochemicals and hormones are released. However the breakthrough came in 1976, soon after the discovery of endorphins. Two groups, one studying human volunteers (Mayer 1977), the other working on animals (Pomeranz and Chiu 1976) showed that Naloxone (an endorphin antagonist) blocked AA. The acupuncture-endorphin hypothesis, which emerged, proposed that AA is a result of peripheral nerve stimulation, which sends impulses to the brain to release endorphins and causes analgesia. This hypothesis, more than any other, has stimulated research in dozens of laboratories on 4 continents (Pomeranz and Stux 1988). Prof. Bruce Pomeranz laboratory was one of the first to show that acupuncture was mediated by endorphins. He began his work with spinal cord experiments in anaesthetised animals. Recording from single cells involved in nociceptive transmission from spinal cord to brain he showed that electroacupuncture analgesia blocked the message and that this effect was prevented by Naloxone, the endorphin antagonist. In another series of experiments he showed that intrathecal naltrexone only blocked when injected before acupuncture treatment began, but could not block analgesia if given after completion of the acupuncture treatment (Pomeranz and Stux 1988).

Professor Le Bars's (1979/89) group in Paris showed that pain in one part of the body inhibits pain responses in another part. When

observed on spinal cord dorsal horn wide dynamic range neurons this effect was called DNIC (diffuse noxious inhibitory control) when observed in rats, or with flexor withdrawal reflexes in humans they called it 'counterirritation'. Whether or not DNIC is a model for acupuncture however is unclear, as unmyelinated 'C' fibres are activated for the conditioning stimulus, whereas acupuncture generally activates myelinated 'A-delta' and Type III muscle afferents. The De Qi sensations produced by acupuncture being a mild ache and not frank pain. Also the time course of DNIC is a matter of controversy; it shows a rapid onset and short after-effect, starting immediately and lasting only several minutes after conditioning stimulus ends. Acupuncture has a much longer induction time and after-effect taking 5-30 minutes to get going, and outlasting the treatment by 20 minutes to several hours (Pomeranz and Stux 1988). The counterirritation experiments conducted in humans had a much more appropriate time course for a model of acupuncture than the DNIC experiments in rats. Moreover, the human experiments were very convincing because of the elegant correlation of flexor reflex suppression (measured by sural evoked reflex EMGs from biceps femoris) and psychophysical measures of sensory analgesia produced by counterirritation. The subjects dipped their arm into hot water (above 45° C) for several minutes to produce counterirritation. This produced analgesia, which had after-effects lasting 10-15 minutes. The effect was blocked by Naloxone (pretreatment), and was absent in paraplegic patients (Pomeranz and Stux 1988). Professor Ulett's (1989) work showed that acupuncture is as effective as morphine or hypnosis in suppressing pain in human volunteers. Since hypnotic susceptibility did not correlate with acupuncture success rate, the two are not the same phenomena (a result confirmed by others using Naloxone antagonists which block acupuncture but not hypnotic analgesia (Pomeranz and Stux 1988). Altogether one can conclude that low-frequency electroacupuncture analgesia depends on the release of beta-endorphins in the brain and met-enkephalins in the

spinal cord, whereas high-frequency analgesia is mediated by dynorphins in the spinal cord (Han 1989).

3.5.5 Methods of Administration

The most popular methods of electrical treatment at this time are electroacupuncture and conventional and acupuncture-like transcutaneous electrical nerve stimulation and these modes of application are considered as follows and summarized in Figure IX:

1. **Electroacupuncture (EAP):** in 1958 when the Chinese were developing methods of acupuncture for surgical anaesthesia, which necessitated long periods of manual manipulation, it was found to be more effective to stimulate the needles electrically by attaching flexible wires, via small crocodile clips, to the needles from a pulse generator. Electroacupuncture was reborn (see 3.2) and later introduced into clinical practice on a more general basis for the treatment of pain and neurological disorders. Usually 4-8 needles can be stimulated at one time via parallel channels on the stimulator. One pair of needles inserted into an acupuncture point, wires and a pulse generator outlet is required to complete one circuit. Pulses of electricity are applied to the needles in order to stimulate nerves via the acupuncture point. In order to achieve an optimum effect for EAP, the strongest tolerable intensity is recommended by Pomeranz (1991) for De Qi.
2. **Acupuncture-like Tens (ALTENS):** is a treatment mode given without the use of needles using low-frequency, high intensity treatment currents. Small flexible electrode pads consisting of electroconductive carbon-filled vinyl sheets (as supplied with conventional TENS units) are applied to the skin over an acupuncture point. The electric current is then applied until the nerves are activated transcutaneously. A much higher

current/voltage is required than with EAP because of the greater surface area of the electrodes and the greater intact skin resistance. ALTENS is a safer treatment modality eliminating the risks of infection, bruising, organ damage and pneumothorax, needle breakage's, fear of needles, etc. There are few disadvantages to this mode of treatment provided a suitable biphasic unit is used such as the Equinox or VTENS machines. Body or ear punctate treatments are best performed with a suitable point stimulator such as the 'Solitens/Stimplus II' unit but they can be carried out with the above treatment units using the crocodile clip as the electrode.

3. Conventional TENS: conventional TENS is based on similar units, but these are often monophasic or asymmetrical biphasic as described above, but using a much higher frequency range i.e. 50-200 pps and more and at a low intensity, therapeutically, pain relief is by activation of low-threshold cutaneous afferents (type I and A beta) and is based on the Gate Theory of pain. This form of pain relief starts within a few moments of TENS stimulation and usually disappears within a few seconds of switching the machine off. Hence, TENS must be used for long periods throughout the day to obtain sustained relief. Conventional TENS is mainly segmental in nature and does not appear to involve pituitary mechanisms. In conclusion, ALTENS appears superior to conventional TENS (and many practitioners consider it superior to EAP) because it produces prolonged analgesia, has very few side effects, only requires a 30 minute session once a day or once/twice a week for maximum therapeutic effects. The major differences between conventional TENS and acupuncture-like ALTENS is summarized in the following Figure IX (after Stux and Pomeranz 1995).

Conventional TENS	Acupuncture-like TENS
High frequency, low intensity, Gate control theory mechanism.	Low frequency, high intensity, De Qi.
Low intensity activates large muscle (type I) and large skin (A β) nerves for Gate effect	High intensity pulses produce De Qi via small muscle (type III) nerves to release endorphins.
Segmental effects based on Gate Theory: large diameter fibres inhibit pain from small fibres.	Nonsegmental and segmental effects: small fibres act on three sites: spine, brainstem and pituitary.
High intensity of most TENS devices causes burning from skin but no De Qi from muscle.	High intensity of some TENS devices activates small muscle (type III) nerves producing De Qi
Pads are placed near the site of pain as large diameter fibres are widely distributed	Pads placed on acupuncture points as these are over small diameter afferent nerves (type III) in muscle.
High frequency (50-200 Hz) produces best presynaptic inhibition at low intensity (for Gate) but produces spasms at high intensity	Low frequency (1-4Hz) produces no muscle spasm at high intensity and hence allows strong stimulation needed for De Qi.
Trains maximise comfort of low intensity, high frequency stimulation.	Trains cause muscle spasms at high intensity and do not permit adequate intensities for De Qi
Analgesia has rapid onset and short duration requiring continuous treatment all day long.	Analgesia has slow onset and long duration: needs only 30 minutes of therapy for prolonged effects
Tolerance develops from continuous therapy.	No tolerance from short, 30 minute treatments.

Figure IX: Table of comparisons of the two methods for TENS from Pomeranz and Stux (1995)

3.5.6 Treatment Parameters

Research on animals and human volunteers shows that it takes 20-30 minutes for endorphinergic analgesia to build up, and typically the preparation for surgical 'anaesthesia' takes 30 minutes of stimulation (Stux and Pomeranz 1995). This parameter is reflected in the average clinic treatment time of 25-30 minutes. If one is treating according to traditional Chinese medicine, EAP intensities should be determined by the requirement to sedate or to tonify. When sedating high intensity low frequency stimulation is used to achieve De Qi; when tonifying low intensity stimulation (just above threshold) and a higher frequency are used (Stux and Pomeranz 1995). Generally, pain therapy requires sedation at frequencies below 10 pps, usually less than 3pps, but in some patients who are debilitated by chronic pain, tonification above 10 pps may be indicated or a pulse burst mode stimulation at 1 burst per second, with an internal frequency above 10pps and up to 200 or more. In clinical practice it is also popular to use EAP and ALTENS at alternating frequencies of 2 and 15 or 2 and 100 pps or as a pulse burst mode. In this case, both enkephalins, and/or endorphins, as well as dynorphins are released. Clinical experience indicates that the best analgesic effect of electroacupuncture can be obtained when two frequencies (low and high) shift automatically. It also fits well with the synergism between the analgesic effect of met-enkephalins (released by low-frequency) and dynorphins (released by high-frequency electroacupuncture) (Han 1989).

Following on from and in support of the above are the following study descriptions. The first of which describes a randomised placebo controlled trial of the analgesic effect of electroacupuncture, which was compared to that of placebo electroacupuncture, using low frequency high intensity transcutaneous electrical nerve stimulation, in 14 patients with chronic non-cancer pain. Patients underwent six

randomly assigned treatment sessions, each lasting 20 minutes, at least 48 hours apart: two sessions of classical acupuncture, two sessions of placebo electroacupuncture using non-acupuncture points, and two sessions using surface electrodes placed over painful sites. For all sessions, current was set just above pain threshold, at a pulse width of 200ms and a pulse rate of 2Hz. Pain ratings were determined before and immediately after stimulation and at intervals during the subsequent 48 hours. Five of the 14 patients demonstrated significant improvement in pain with all three types of stimulation. There was no significant difference in the degree or duration of analgesia achieved among the three modalities, suggesting that classical electroacupuncture is no more effective than other forms of low frequency high intensity stimulation (Abram 1983). These findings, from nearly fifteen years ago, also support the current trend towards the practice of electro-stimulation using surface electrodes rather than needles and which is now known as acupuncture-like TENS. The thesis author, in his placebo controlled randomised trial described in section 3.6, also used this mode of electro-stimulation.

Secondly, recent studies in anaesthetised rats, show that two successive acupuncture treatments given for 15 minutes (or preferably for 25-30 minutes) 90 minutes apart cause a potentiation of acupuncture analgesia. Moreover, naltrexone blocks the AA only if given prior to the first acupuncture treatment. This suggests that the first endorphin effect modulates the synapses so that the second AA (which need not be endorphinergic) is more powerful. This cumulative AA effect of repeated acupuncture treatments has been known for years anecdotally, but has been recently documented clinically (Price 1984). Hence unlike conventional TENS which must be used continuously because of transient effects, acupuncture and acupuncture like-TENS, need only be given 30 minutes a day because of prolonged after-effects, and the cumulative build-up of potentiation from repeated treatments (Pomeranz 1989). One possible explanation for the prolonged benefit stemming from this protocol could be that

acupuncture releases ACTH along with the pituitary endorphins. In a study in awake horses, elevated blood cortisol levels were measured after true acupuncture, but no change observed after sham needling. The latter ruled out the possibility that stress was the mediating factor. Perhaps the cortisol produces anti-inflammatory effects in chronic pain due to arthritis, and thus produces 'cures'. Another possibility is that the cumulative endorphin effects may permanently change the pain circuits (Pomeranz 1989).

3.5.7 Discussion

In addition to the lack of a plausible mechanism to explain acupuncture analgesia, sceptics were concerned about the anecdotal nature of acupuncture and electro-acupuncture claims. Despite the huge size of the anecdotal database (one quarter of the world's population had been using acupuncture for 2500 years for pain and other non-painful applications) sceptics were calling for controlled clinical studies to prove the efficacy of acupuncture (Pomeranz and Stux 1988). A growing body of research published in the last 20 years shows that acupuncture analgesia (AA) is very effective in treating chronic pain, helping from 55% to 85% of patients (Lewith 1982; Richardson and Vincent 1986; Vincent and Richardson 1986), which compares favourably with drugs. Moreover the evidence shows that in placebo control groups only 30% of cases were helped, establishing that AA is more effective than placebo and that AA is a real physical effect. In addition to the clinical studies, which demonstrate efficacy, another way to overcome the deep scepticism towards acupuncture was to establish credible physiological mechanisms of action (Pomeranz and Stux 1988). Some writer's note that there are several studies, (at least seven) which failed to observe Naloxone effects on acupuncture analgesia. This is against 28 papers showing Naloxone blockade of acupuncture analgesia. The reasons for the failed Naloxone experiments are not always clear. However, three of the

failed Naloxone experiments were observed with high-frequency, low intensity stimulation, whereas in several animal studies it was found that AA-endorphin mechanism operates best with low frequency (4 pps or less) and high intensity stimulation. This has also been confirmed in man. In one of the failed experiments, low frequency, low intensity was employed with an absence of 'De Qi'. The reasons for the remaining failed Naloxone experiments might be a recently discovered feature of endorphinergic analgesia: Opioid antagonists seem to work best when given before the treatment begins and fail to reverse analgesia that has already been initiated (Pomeranz 1989). So it appears from these observations that Naloxone can prevent but cannot reverse acupuncture analgesia.

In the early days following the discovery of endogenous opioids, people were hoping for a new group of analgesics without the drawbacks of morphine, e.g. without tolerance and dependence. These expectations, however, soon vanished since administration of a large amount of synthetic opioid peptides caused tolerance and dependence in a way similar to morphine. If electroacupuncture (and acupuncture-like TENS) releases endogenous opioids to exert an analgesic effect, one would expect that electroacupuncture analgesia also leads to the development of tolerance, when applied continuously or repeatedly with short intervals (Han 1989). Clinical practice, however, does not support this theory.

It is noted that peripheral tissue damage or nerve injury often leads to pathological pain processes, such as spontaneous pain, hyperalgesia and allodynia, that persist for years or decades after all possible tissue healing has occurred. Although peripheral neural mechanisms, such as nociceptor sensitisation and neuroma formation, contribute to these pathological pain processes, recent evidence indicates that changes in central neural function may also play a significant role. Coderre (1993) examined the clinical and experimental evidence which points to a contribution of central neural plasticity to the development of pathological pain, and assessed the

physiological, biochemical, cellular and molecular mechanisms that underlie plasticity induced in the central nervous system in response to noxious peripheral stimulation. They conclude that clinical and experimental evidence suggests that noxious stimuli sensitise central neural structures involved in pain perception e.g. phantom limb pain. An increased understanding of the central changes induced by peripheral injury or noxious stimulation should lead to new and improved clinical treatment for the relief and prevention of pathological pain (Coderre 1993). I would suggest that electroanalgesia in the form of ALTENS may be this new mode of clinical treatment, especially in view of the beneficial effects of reducing or eliminating long standing pathological pain, and the effects of electrostimulation on central neurotransmitters and their role in pain relief.

So in summary, electro-acupuncture and acupuncture-like TENS uses low frequency high intensity stimulation, below 4pps to prevent muscle spasms, to stimulate the production of enkephalins and dynorphin at a segmental level and beta-endorphin, dynorphin and serotonin at non-segmental levels i.e. brain stem and hypothalamus-pituitary. Conventional TENS uses high frequency low intensity stimulation, usually 50-200pps, as this promotes the optimum presynaptic inhibition through the Gate mechanism (presumably using gamma-aminobutyric acid GABA together with some dynorphin release (Han 1991)) and is therefore mainly segmental in nature, not involving pituitary mechanisms. On the whole, acupuncture-like TENS appears superior to conventional TENS (in theory and in everyday practice too) because it produces prolonged analgesia and thus the stimulator does not have to be worn continuously by the patient. Acupuncture-like TENS treatment, in skilled hands, can relieve both acute and chronic pain and is capable of eliminating pain of many years duration. One 30-minute treatment session a day (or even once or twice a week) is sufficient therapy using acupuncture-like TENS for chronic pain. This is similar to the

experience with acupuncture analgesia in which prolonged effects are achieved (Stux and Pomeranz 1995).

This section has drawn heavily on the recent and ongoing work of Professor Bruce Pomeranz from Toronto, one of a small number of prominent neuroscientists deeply involved in finding out how acupuncture and electrostimulation in particular works. He recently presented these findings in London, in October 1996, and one of my colleagues David Mayor attended this seminar and he gives a full account of his lectures in a recent paper (Mayor 1997) which also confirms my assessment of the literature as described above.

Having set the scene in the first four sections of this thesis, the final section of this stage is a piece of clinical research, as a pilot study, based on the findings discussed in this section of the thesis. The study takes the form of a randomised placebo controlled trial of electroanalgesia in palliative medicine, using acupuncture-like transcutaneous electrical nerve stimulation and is described in full in section 3.6 which follows.

3.6: Clinical Research: A Randomised Controlled Trial of Electroanalgesia in Palliative Medicine using Acupuncture-like Transcutaneous Electrical Nerve Stimulation: A Pilot Study

3.6.1 Introduction

This study originated following informal discussions between Dr Ian Johnson, then Consultant in Palliative Medicine at The Leicestershire Hospice, and the author J Gordon Gadsby with their mutual interest in acupuncture and related electrical therapies in relation to antiemesis and analgesia in palliative care. After prolonged discussions a research protocol, questionnaires, consent forms and patient information documents were prepared a priori, in the form of a study manual which was used as the reference document during this trial, and is included in Appendix A(i).

An application for research ethics approval was made to the Committee on the Ethics of Clinical Research Investigation of the Leicestershire Health Authority and this application form is enclosed as Appendix A (ii).

Academic and scientific supervision was provided by Dr Frank Dewhurst, Deputy Head of the Department of Biological Sciences, and statistical supervision by Mr Philip Jarvis of the Department of Medical Statistics of the De Montfort University Leicester. Dr Alison Franks took over the clinical supervision from Dr Ian Johnson on his departure from the Leicestershire Hospice.

It was anticipated that on completion of the pilot study, approval would then be sought for a full scale trial, based on the power estimations discussed in the following text, however, this was not pos-

sible because of the medical and nursing politics of the situation and the lack of adequate funding resources.

Unfortunately, this trial had to be terminated on completion of the pilot study for the reasons given above and the implications for this are discussed in more detail later in this section. However, the strengths of the trial methodology coupled with the preliminary findings of this study were considered suitable for publication in the *Journal of Complementary Therapies in Medicine* after peer review.

In order to demonstrate these strengths and the preliminary findings of this pilot study, the format of the next part of this section is based on the recent publication of the above study referenced as:-

Gadsby, J.G., Franks, A., Jarvis. P., Dewhurst F. (1997) Complementary Therapies in Medicine Vol 5, pp. 13-18.

The numerical referencing from the original paper has been changed to the Harvard style, in keeping with the rest of this thesis, but the content reflects the above publication in all its detail.

3.6.2 Title: Acupuncture like transcutaneous electrical nerve stimulation within palliative care: a pilot study.

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De Montfort University, Leicester and The Leicestershire Hospice, UK.

3.6.3 Summary

Objective: To determine the potential role of acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in helping to improve the quality of life for patients in a palliative care setting.

Design: Double-blind randomized controlled trial.

Setting: Leicestershire Hospice.

Patients: 15 patients admitted for symptom control. **Interventions:** Patients randomly allocated to receive standard treatment, standard plus ALTENS or standard plus placebo.

Main Outcome Measures: EORTC QLQ-C30 Quality of Life Questionnaire.

Results: The symptoms of pain and nausea and vomiting were not improved in this pilot study. The symptoms of fatigue showed some improvement, the relative risk of this improvement being 8 times that of placebo and 16 times that of standard controls. The overall quality of life was also improved, the relative risk being twice that of placebo and 2.67 times that of standard controls.

Conclusions: It is difficult to draw conclusions on the basis of such a small pilot study but the initial indications suggesting beneficial effects in the quality of life and fatigue symptoms would appear to warrant further investigation.

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3.6.4 Introduction

There have been many studies since the gate control theory of pain was first published by Melzack and Wall (1965), which have shown the effectiveness of transcutaneous electric nerve stimulation (TENS) in the alleviation of pain and other symptoms. This clinical study developed following a consideration of these reports on electrical pain relief within musculo-skeletal and neurological systems (Shealy 1974b, Long 1991, Duncombe 1991, Johnson 1992a/b, Shealy and Maudlin 1994) and in cancer pain (Wen 1977, Ostrowski 1979, Ventafridda 1979, Avellanosa and West 1983, Rico 1983), and in electrical anti-emesis (Dundee 1989ab/1990ab/1991abcde/ 1992ab, Evans 1993, Ghaly 1987, McMillan 1991abc/1993) which also appeared beneficial to patients. The use of this modality within palliative care and in symptom control seemed a logical progression, there being little current data available from randomized controlled trials to support its use in this area. There are few ethical objections to these treatments since they are known to be very safe with few contraindications. This study used the technique of acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) as an adjuvant therapy to conventional antiemetic and analgesic medications. It was anticipated that the application of this treatment would enhance the effectiveness of both conventional antiemetics and analgesics, with an hoped for reduction in their usage together with an overall improvement in the quality of life as measured by the EORTC QLQ-C30 (European Organization for the Treatment and Research of Cancer, Quality of Life Questionnaire) as described by (Sprangers 1993, Anderson 1993, Aaronson 1993). The EORTC QLQ-C30 is a quality of life instrument designed for use in clinical trials and has already been used in several international clinical trials in oncology (Ringdal 1993, Niezgoda and Pater 1993, Calais de Silva 1993). It incorporates nine multi-item scales: five functional (physical, role, cognitive, emotional and social); three symptom (fatigue, pain and nausea and vomiting); and a global

and quality-of-life scale that reflect the multidimensionality of the quality-of-life construct. Several single-item measures are also included. The pain, fatigue, nausea and vomiting symptom scales employ four-point Likert-type response categories and refer to perceptions 'during the past week'. All subscale scores may also be linearly converted to a 0-100 scale and a lower score after treatment reflects a lower level of symptomatology. The above studies support the EORTC QLQ-C30 as a reliable and valid measure of the quality of life in cancer patients in multicultural clinical research settings. It is a copyright instrument and a User's Agreement was sought from the EORTC Quality of Life Group to use this questionnaire for this study only together with a key-scoring algorithm for analysis.

3.6.5 Patients, materials and methods

Every patient entering the unit between August and November 1994 for symptom control and who met the eligibility criteria were entered into the trial. The inclusion criteria were that patients should have pain and/or nausea and vomiting symptoms, age range 35-75 and are of Caucasian origin. Exclusion criteria included all patients unwilling to provide informed consent, those too ill to cope with 30 minutes of treatment, patients with an on-demand pacemaker, pre-menopausal women, patients with vomiting due to intestinal obstruction or raised intracranial pressure or iatrogenic causes and those who had previously received TENS or ALTENS treatment. Patients were entered into the trial following an independent assessment by a clinician and completion of a consent form, the EORTC QLQ-C30 and a WHO performance status score. There were 14 female and 1 male patient with ages ranging from 38 to 74 years and with a diagnosis of terminal cancer, comprising 6 breast, 3 colon, 2 pancreas, 2 kidney, 1 stomach and 1 cervical.

On entry patients were randomly allocated trial therapies, via the sealed envelope method of colour coded allocation cards to receive ac-

tive ALTENS, placebo ALTENS or no ALTENS (“no ALTENS” standard control) in addition to recognised standard therapies for pain and antiemesis. They then proceeded to five consecutive daily treatments given by the nurse practitioner (JGG) as follows:

1. Daily biophysical measurements of body electrical resistance readings pre and post treatment were taken using a standard multimeter and hand held electrodes and recorded on the data collection sheet.
2. Daily real or placebo ALTENS treatments were given, using a colour coded system of leads corresponding to the colour code allocation card. One pair of lightly gelled carbon vinyl electrodes 4 cm² were attached to the patient, one to the acupuncture point Pe6 (Neiguan) and one to the point LI4 (Hegu) of the dominant hand (and secured with tape).
3. The use of acupuncture points Pe6 for electro-antiemesis is well accepted in the literature as described above (see Dundee references) and the use of LI4 for electro-analgesia is a standard procedure both within Traditional and Western acupuncture systems (Lapeer 1986, Stux and Pomeranz 1987, Aung 1993). The leads were then attached to a V-TENS_{TM} stimulator and the unit switched on.

The electrical parameters were as follows: -

- (a) pulse rate set at 2 pulses per second with a symmetrical biphasic pulsewave in continuous mode.
- (b) pulse width 200 microseconds.
- (c) amplitude setting at 2.5 on the unit output scale.
- (d) timer set at 30 minutes as the duration of each treatment.



4. On day 6 a second EORTC QLQ-C30 was completed together with a retrospective assessment of analgesic and antiemetic use over the study period and recorded on the data collection sheets.

Outcomes were measured using the differences between the pre and post treatment EORTC QLQ-C30 questionnaires in respect of the three symptoms of pain, nausea and vomiting and fatigue, the global quality of life and the five functional scales together with a retrospective evaluation of drug use during the five day period.

The Kruskal-Wallis test was applied to the differences in the global quality of life as a total score and also to the three major symptoms of terminal cancer i.e. nausea and vomiting, pain and fatigue. The null hypothesis was that the medians of the three populations were equal with the alternative that they were not. No statistically significant differences between the three groups could be detected. The tests were computed using the Minitab statistical software program. Descriptive statistics were computed and inferences of treatment effects using 2 x 2 tables of counts were then performed on the global quality of life, nausea and vomiting scores, pain levels and fatigue scores and the odds ratios (approximate relative risks) were calculated. The odds ratio permits a direct comparison of the odds of improvement on one treatment compared to another treatment. Conventionally, odds ratios greater than one are used for 'positive results' i.e. the risk is taken to mean risk of improvement.

Quality Control: The output leads were colour tagged, real and placebo, and the code changed at bi-weekly intervals during the study in order to help maintain the double-blind element. A second independent observer who kept a record of the codes throughout the trial undertook this. Using a standard multimeter, a daily quality control check on battery charge was made before the commencement of each treatment. There was minimal interpersonal interaction between the nurse practitioner and the patient to reduce operator bias and to maintain the double-blind condition.

3.6.6 Results

Fifteen eligible subjects were entered into this study, five into each arm (real, placebo or standard treatment). The groups were all similar prior to the intervention Each group began the study with five subjects however complete data on all outcome measures were available

Figure X: Tables of Baseline Characteristics and Post-Treatment Scores

No. ALTENS	Age	Sex	Diagnosis	Global baseline scores	Global post- treatment	Fatigue baseline scores	Fatigue post- treatment	Nausea/ Vomiting baseline	Nausea/ Vomiting post	Pain baseline scores	Pain post- treatment
1	74	F	BREAST	89	74	4	3.67	2.5	1.5	2	1.5
2	62	F	BREAST	75	76	3	3	2.5	2	4	4
3	68	F	BREAST	81	77	3.3	3	1	1	4	4
4	38	F	CERVIX	83	77	4	2.67	2.5	4	2.5	3
5	63	F	KIDNEY	90	85	3.34	2.67	3	1.5	3.5	3.5

Placebo

6	72	F	BREAST	76	53	3.67	2	1	1	3.5	2
7	58	F	LUNG	68	78	2	3	4	4	1	1
8	68	F	BREAST	80	77	2.67	3.34	3	3.5	3.5	4
9	74	F	PANCREAS	(53)	-	2	-	3	-	1.5	-
10	69	F	COLON	(73)	-	3.34	-	3	-	1	-

Control

11	58	M	KIDNEY	78	58	3.67	2.34	2.5	2	3	1.5
12	58	F	BREAST	74	73	4	4	2	2.5	2	2
13	70	F	COLON	86	97	3	4	3	4	3	3
14	61	F	BREAST	94	83	3.67	3.67	4	1	3	1.5
15	65	F	PANCREAS	91	77	3.67	4	4	2	3.5	1.5

for only 13 subjects, (all on ALTENS, all in the control group, but only three in the placebo ALTENS group). Two patients in the placebo group were unable to complete the second EORTC QLQ-C30 due to a rapid deterioration in their condition (Figure X).

- 1. Descriptive statistics for the overall quality of life are shown in Figure XI. The Odds Ratio calculation for ALTENS being 2.67 times that of the control and that of the placebo to control 1.33 times (see also Appendix III, pages 409-410, for tables of odds ratios for 1,2,3 and 4).
- 2. Descriptive statistics for the symptoms of fatigue are shown in Figure XII. The Odds Ratio calculation for ALTENS being 16 times that of the control and that of placebo to control 2 times.
- 3. Descriptive statistics for the symptoms of nausea and vomiting are shown in Figure XIII. The Odds Ratio calculation for ALTENS being 9 times that of the control and that of placebo to control the same.
- 4. Descriptive statistics for the symptoms of pain are shown in Figure XIV. The Odds Ratio calculation for ALTENS was 0.5 times greater than that of the control and that of placebo to control 0.16 times.

Figure XI: Table of descriptive statistics for the global quality of life.

Quality of Life	ALTENS	Placebo ALTENS	CONTROL
Baseline Scores	Mean = 83.6 SD = 6.15	Mean = 74.7 SD = 6.11	Mean = 84.6 SD = 8.47
Post-treatment Scores	Mean = 77.8 SD = 4.21	Mean = 69.3 SD = 14.15	Mean = 77.6 SD = 14.24
Pre-Post Dif- ference Scores	Mean = 5.8 SD = 5.81	Mean = 5.33 SD = 16.62	Mean = 7.00 SD = 12.19

Figure XII: Table of descriptive statistics for the symptoms of fatigue.

Fatigue symptoms	ALTENS	Placebo ALTENS	CONTROL
Baseline Scores	Mean = 84.44 SD = 14.91	Mean = 59.3 SD = 28	Mean = 86.67 SD = 12.17
Post-treatment Scores	Mean = 66.67 SD = 13.61	Mean = 59.3 SD = 23.1	Mean = 86.7 SD = 24.1
Pre-Post Difference Scores	Mean = 17.78 SD = 16.85	Mean = 0.00 SD = 48.4	Mean = 0.00 SD = 28.3

Figure XIII: Table of descriptive statistics for the symptoms of nausea and vomiting

Nausea/ vomiting	ALTENS	Placebo ALTENS	CONTROL
Baseline Scores	Mean = 43.3 SD = 25.3	Mean = 55.6 SD = 50.9	Mean = 70.0 SD = 29.8
Post-treatment Scores	Mean = 33.3 SD = 39.1	Mean = 61.1 SD = 53.6	Mean = 43.3 SD = 36.5
Pre-Post Difference Scores	Mean = 0.30 SD = 1.15	Mean = -0.167 SD = 0.29	Mean = 0.80 SD = 1.68

Figure XIV: Table of descriptive statistics for the symptoms of pain.

Pain symptoms	ALTENS	Placebo ALTENS	CONTROL
Baseline Scores	Mean = 78.3 SD = 30.3	Mean = 55.6 SD = 48.1	Mean = 63.33 SD = 18.26
Post-treatment Scores	Mean = 73.3 SD = 34.6	Mean = 44.4 SD = 50.9	Mean = 30.00 SD = 21.73
Pre-Post Dif- ference Scores	Mean = 0.00 SD = 0.35	Mean = 0.33 SD = 1.04	Mean = 1.00 SD = .935

5. Patients on ALTENS and placebo treatment had recordings of their electrical resistance in kilohms (kΩ) taken in order to make a comparison with average normal readings taken from people not suffering from cancer. The average normal readings from people in good health, taken via hand held electrodes and a standard multimeter, have been found to be in the range of 15-20 kΩ. Patients on ALTENS had pre-treatment average recordings of 543 kΩ and post-treatment averages of 423 kΩ (Figure XV).

Figure XV: A comparison table for hand to hand electrical resistance readings taken from normal and trial subjects.

	PRE-TREATMENT	POST-TREATMENT
NORMAL	15kΩ	-
ALTENS	543kΩ	423kΩ
PLACEBO	502kΩ	418kΩ
GLOBAL	522kΩ	420kΩ

Patients on placebo treatments had pre-treatment average recordings of 502 k Ω and post-treatment averages of 418 k Ω . The global average recordings pre-treatment were 522 k Ω and post-treatment 420 k Ω . In comparison with the average normal reading of 15 k Ω these recordings show an electrical resistance 28 - 34 times normal.

3.6.7 Discussion

The aim of this study was to start to assess whether there may be a role for acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in helping to improve the quality of life for terminally ill patients. ALTENS is delivered by a low frequency high intensity treatment current (below 10 pulses per second and usually below 3) in comparison with conventional TENS which has a high frequency low intensity treatment current (above 10 pps and usually between 80-100). The rationale is that ALTENS treatment at 2 pps for 30 minutes shows a marked increase in beta-endorphins (Abenyakar 1994), and met-enkephalins (Han 1991), whereas TENS treatment at 80-100pps does not produce this increase (Abenyakar 1994) but an increase in dynorphin A (Han 1991). However it is more widely accepted that conventional TENS is based on the gate theory of pain (Melzack and Wall 1965) and recent research appears to confirm this mechanism more clearly (Garrison and Foreman 1994).

The main objectives of this study were to assess the effectiveness of this non-invasive therapy, as an antiemetic and analgesic, as an adjunct to conventional care, and secondly to record biophysical measurements of electrical resistance in cancer patients and to compare them with measurements in non-cancer controls. The results outlined above did not reach statistical significance and if ALTENS did have an effect on pain or nausea in palliative care, it is doubtful that a study with 5 patients per arm would be large enough to detect it. The trial is underpowered and so there is a high probability that it may have failed to detect differences, particularly in view of the heteroge-

neous population. However, it is suggested that the therapeutic responses to ALTENS observed in this trial are worthy of further investigation within a larger trial.

The initial observations and analyses would also appear to support the theory that recording biophysical measurements of electrical resistance in cancer patients and in comparison with measurements in non-cancer controls indicate significant differences, the implications of which are not fully known, but which are the subject of further investigation at this time. It had been suggested that the high electrical resistance readings of terminally ill patients may be due to a high intake of opiate medication but this was not supported by a comparison of the retrospective dose drug estimations for individual patients. It was also expected that the three randomly assigned treatment groups at baseline would have no significant differences. However, it appears, from the retrospective drug estimations, that patients assigned to the real treatment were taking significantly larger quantities of daily opioids than those receiving the placebo or the standard control.

The double-blind condition cannot easily be maintained in trials of physical treatments, and trials of acupuncture for example are often single blind design (Vincent 1989, Dundee 1992a). However, one of the strengths of this study is that it appears to have fulfilled the double-blind criteria, and with an additional non-treatment control arm which was seen as a credible, bona fide treatment by patients. The high electrical skin resistance of these patients appeared, on questioning the patient for the level of comfort by the trialist, to be blocking the sensory stimulation of the ALTENS from reaching conscious awareness. This blocking of sensory awareness and the communication of such between patient and trialist also helped to reduce the risk of operator bias. It therefore seems likely that this study is one of the first trials of a physical modality that can be said to meet the requirements of a double-blind randomized controlled trial. Other researchers may consider the implications of this important observa-

tion for further physical therapy studies with this group of patients. However, it is feasible that the high levels of skin resistance found in these patients could have lowered the effectiveness of ALTENS and in the clinical situation the intensity of stimulation would have been raised to patient tolerance.

Statistical methods of power calculations were then used to determine the required number of patients to meet the trial's outcome in respect of the fatigue symptoms which was the only outcome of significant interest. For an 80% chance of demonstrating a difference in the 'fatigue difference' of 0.54 and to be statistically significant at the 2-sided 5% level, a sample size of 48 patients/group (a total of 144 patients) would be required. However, it was considered that a further trial based on these sets of numbers was beyond the resources of the research team at this time and the trial was ended.

Finally, whilst the pilot study showed several interesting observations within palliative care mainly in respect of the symptoms of fatigue, the main objectives of using acupuncture-like transcutaneous electrical nerve stimulation to alleviate pain and nausea and vomiting were not demonstrated within this small pilot study. The observations on the treatment of fatigue were, however, most interesting and may have wider implications within the field of chronic fatigue states and may also help to explain the improvement many patients with myalgic encephalomyelitis, post-viral fatigue syndromes, functional chronic fatigue states, fibromyalgia and other fatigue states of known or unknown cause, experience after a course of ALTENS or electroacupuncture using high intensity low frequency stimulation.

In the light of these preliminary findings it is suggested that further trials of ALTENS are indicated both within palliative care and within chronic fatigue states by both orthodox and complementary medicine researchers.

3.6.8 Acknowledgements

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3.6.9 Conclusions

The author has presented this clinical research study, using the publication format of the Complementary Therapies in Medicine Journal (Gadsby and Franks 1997) in order to demonstrate the characteristics, methodology and results of this placebo controlled randomized clinical trial in the form of documentation which has been subject to peer review and subsequently published as a research paper. As stated earlier, it was our original intention to proceed with a full scale study, based on the protocol identified in the Manual, and on completion of the pilot study, but this was deemed not to be possible within the resources of the research team at that time. This study from conception to completion had taken more than 12 months of concerted effort.

In the interim, however, the author became aware of and increasingly interested in the development and aims of the newly established Cochrane Collaboration and the conduct of tertiary research within this framework. In consultation with academic supervisors it was decided to approach and seek to join the Cochrane Collaboration in order to carry out a programme of tertiary research, at doctorate level, as a Systematic Review and meta-analysis of the effectiveness of electrical stimulation in the treatment of chronic back pain.

3.7: Conclusions and Recommendations on Completion of the First Stage of the Thesis

On completion of the first stage of the programme of research, described in section 3 (3.1-3.6), an interim report was prepared and submitted to the Research Degrees Committee of the De Montfort University in accordance with the Research Degree Regulations of De Montfort University (September 1994) in order to seek a Transfer of Registration between M.Phil. and Ph.D.

The interim report is reproduced in its entirety in Appendix A with original referencing. This report was based on the programme of completed research at the time of writing (September 1995). It was almost inevitable that as the doctoral programme of study evolved some changes would also take place but in essence the main aspects of the research programme for the doctoral programme of study remains unchanged apart from the areas discussed below:-

1. The initial stage of the research programme had already been completed but strengthening and consolidation of this research continued over the next two years via the search for new information and by seeking publication of several elements of this research as referenced later in section 5.
2. The main elements of the doctoral stage of tertiary research were developed beyond the initial aims to produce a Cochrane Review. As this research developed it became clear that an examination by summary of the methodology surrounding the Cochrane Collaboration and systematic reviews would be desirable (in order to reduce the 40,000 word manual to a more manageable document of less than 10,000 words) as a learning process for the author. This was completed together with a practical commentary by the author and the aim now is to make this information available to other collaborators, via the Internet and the Cochrane collaboration e-mail mailing list (CCINFO). This investigation also included the new methodology available to improve and update electronic reviews within the framework of the Co-

chrane Collaboration. This extension and restructuring of the tertiary research project necessitated the loss of the following elements identified in the original research plan:

1. To produce by 1996 a state of the art electrostimulation unit, with electrical parameters based on the findings of this thesis, was abandoned due to the lack of time and financial resources for its development.
2. To maintain, promote and develop still further an evidence-based electroanalgesia training package, which would build on the original documentation produced by the author and which has been in operation for the past four years as a training document for medical and para-medical practitioners, was also abandoned. This project to place electroanalgesia on a sound scientific basis continues but not within the boundaries of this research study at the time of thesis completion. However, this project remains an area for further development in the future.
3. The contemporary applications of electroanalgesia to be written up within a systems format as described earlier was also abandoned in view of the enormity of the project. However this project may be pursued later in view of the resources already collected for assessment.
4. The intention to research the comparative developments between the Society of Electrotherapists and The Society of Chemists was also abandoned due to the demands of the rest of the research programme.

The Research Degrees Committee of the De Montfort University approved the proposals contained in the Interim Report and a Transfer of Registration between M.Phil. and Ph.D. was enacted in order for the post-graduate student to proceed to the doctoral programme of study. The above text, which also describes the changes to the structure as the research programme evolved, completes this stage of the thesis as it moves on to the doctoral programme of study (Section 4) in the form of a tertiary research programme using the tools of Systematic Review and Meta-Analysis.

4.

Tertiary Research Section

Systematic Reviews and Meta-analysis

4.1 Introduction

This section of the thesis builds on the initial research in order to develop and construct a systematic review and meta-analysis of the effectiveness of electroanalgesia in the treatment of chronic low back pain, within the framework of the Cochrane Collaboration, and the Back Subgroup of the Cochrane Musculoskeletal Group (CMSG). [See Appendix B (ia) (ic) (ib) respectively]

The initial research examined the broad historical and contemporary developments of electroanalgesia, the biological and electrical mechanisms of pain and electrical pain relief, and finally an original piece of electroanalgesia research as a placebo controlled randomized controlled trial of acupuncture-like transcutaneous electrical nerve stimulation in the treatment of cancer symptoms, pain, nausea and fatigue, within a palliative medicine setting.

This stage of the research programme greatly enhanced the researcher's insight into the historical and contemporary developments of electroanalgesia, laying down a firm background knowledge base, and the conduct and methodological aspects of the randomized controlled trial were to prove invaluable during the doctoral stage of the research program and the conduct of the Cochrane Systematic Review and Meta-analysis as described in the following subsections of this thesis:

4.2 An examination of the literature and conduct of Systematic Reviews, Meta-analysis and the development of the Cochrane Collaboration.

4.3 Developing a protocol for a Cochrane Review

4.4 Developing a Cochrane Systematic Review and Meta-analysis

4.5 Effectiveness of Transcutaneous Electrical Nerve Stimulation (TENS and ALTENS) for chronic low back pain. A Cochrane Review.

4.6 Improving and updating Systematic Reviews using the Cochrane Collaboration's 'Comments and Criticisms' mechanism.

4.7 Conclusions and recommendations.

4.2 The Cochrane Collaboration, Systematic Reviews and Meta-analysis.

The Cochrane Collaboration is an international organisation that aims to help people make well-informed decisions about healthcare by preparing, maintaining and promoting the accessibility of systematic reviews of the effects of healthcare interventions. Systematic Reviews establish where the effects of healthcare are consistent and research results can be applied across populations, settings, and differences in treatment (e.g. dose); and where effects may vary significantly. The use of explicit, systematic methods in reviews limits bias (systematic errors) and reduces random errors (simple mistakes), thus providing more reliable results upon which to draw conclusions and make decisions. Meta-analysis, the use of statistical methods to summarise the results of independent studies, can provide more precise estimates of the effects of healthcare than those derived from the individual studies included in a review (Mulrow and Oxman 1997:Section1).

The Cochrane Collaboration developed in response to a call by the late epidemiologist Dr Archie Cochrane for systematic up-to-date reviews of relevant Randomised Controlled Trials of health care which need to be kept up to date to take account of new evidence. If this is not done, important effects of health care may not be identified promptly, and people using the health services will be ill-served as a result. Also without systematic reviews of previous research, plans for new research will not be well informed and researchers may embark on studies asking questions that have already been answered (Chalmers 1993).

The NHS Research and Development Programme opened the first 'Cochrane Centre' in Oxford in October 1992 to collaborate with others, in the UK and elsewhere, to facilitate systematic reviews of randomized controlled trials across all areas of health care. The Cochrane Collaboration is a not-for-profit organisation, established as a company, limited by guarantee, and registered as a charity in the UK under the Charities Act 1993. An international response followed a meeting organised by the New York Academy of Sciences with 77 people from nine countries and the 'Cochrane Collaboration was founded. The Cochrane

Collaboration has evolved rapidly since this inauguration and there are now 13 Cochrane Centres world-wide at April 1997.

4.2.1 The eight values of the Cochrane Collaboration

The Cochrane Collaboration's work is based on eight key principles:

1. Collaboration
2. Building on the enthusiasm of individuals
3. Avoiding duplication
4. Minimising bias
5. Keeping up to date
6. Striving for relevance
7. Promoting access by wide dissemination of the outputs of the Collaboration
8. Ensuring quality by being open and responsive to criticism (Hetherington 1997 - also see Appendix B (i)).

4.2.2 Cochrane Reviews and Collaborative Review Groups (CRG'S)

Cochrane Reviews (the principal output of the collaboration) are systematic, up-to-date summaries of reliable evidence of the benefits and risks of healthcare intended to help people make practical decisions and are published electronically in successive issues of *The Cochrane Database of Systematic Reviews*. Preparation and maintenance of Cochrane Reviews is the responsibility of international collaborative review groups and the systematic review to be described in detail later (4.2-4.6) was conducted under the auspices of the Cochrane Musculoskeletal Group (CMSG)- Back Subgroup based in the Institute for Work and Health, Toronto, Canada. By the beginning of 1997 over 40 groups were in existence or planned to cover most of the important areas of health care.

The members of these groups – researchers, health care professionals, consumers, and others – share an interest in generating reliable, up-to-date evidence relevant to the prevention, treatment, and rehabilitation of particular health problems or groups of problems. Each collaborative group prepares a plan outlining how it will contribute to the Collaboration's objectives including its scope and the specific topics falling within the scope, planning, co-ordinating and monitoring the group's work (via the co-ordinating editor, supported by an editorial team), identification and assembling a specialised register of relevant studies, and who will take on the responsibility of preparing and maintaining each review. The day-to-day activities are managed by the group co-ordinator. Training materials are produced by the Collaboration to enable the CRG members to meet their objectives with workshops organised by the Cochrane Centres.

4.2.3 Cochrane Methods Working Groups

The Cochrane Methods Working Groups were created to organise and disseminate the work of methodologists, who come together to improve the validity and precision of systematic review methods, in order to assist reviewers in creating their reviews.

4.2.4 Cochrane Fields

Fields are Cochrane groupings that focus on dimensions of health care other than health problems e.g. care settings, types of consumer, types of intervention etc. Members of fields also co-ordinate the handsearching of journals, compile specialist databases, co-ordinate activities with relevant agencies and comment on systematic reviews relating to their particular area.

4.2.5 Cochrane Centres

The Cochrane centres facilitate the work of the various groups identified above by:

1. maintaining a directory of Collaboration members and their specific interests

2. establish and support CRG's by fostering international interests, discussion groups and organising workshops
3. co-ordinating handsearches of general health care journals and specialist literature
4. co-ordinating an international register of completed and ongoing RCT's in order to facilitate the first phase of data collection for reviewers
5. developing guidelines and software to facilitate the preparation and updating of systematic reviews
6. exploring ways of helping the public, health service providers and purchasers, policy makers and the press to make full use of Cochrane Reviews
7. organising workshops, seminars, and Colloquia to support and guide the development of the Cochrane Collaboration.

The Cochrane centres are not directly responsible for preparing and maintaining systematic reviews. This is the responsibility of CRG's, which also maintains registers of systematic reviews currently being planned, so that unnecessary duplication of effort can be minimised and collaboration promoted.

4.2.6 Consumer participation

An essential part of the Collaboration is the Consumers participation, throughout the organisation, providing input and feedback reflecting consumer interests. This consumer network aims to provide information and a forum for networking; supporting the consumers involvement; provide mechanisms of accountability for consumer representatives in the Collaboration; liase with consumer groups around the world and encourage consumers to become involved in the Collaboration and use its products.

4.2.7 The Cochrane Collaboration and electronic media

The Collaboration provides several software programs, which provides both an organizational and analytic framework for assembling Cochrane Reviews in electronic format.

1. Review Manager (RevMan) is used by reviewers preparing and maintaining reviews.
2. Module Manager (ModMan) is used by the editorial team to assemble protocols and complete reviews prepared by members of the collaborative review group, as well as information about the collaborative review group itself and its specialised register of relevant studies.
3. The Collaboration Parent Database receives modules of Cochrane reviews and information from all the groups, centres, fields, and method working groups registered with the Collaboration.
4. The Cochrane Library is then derived from the information supplied to the continuously updated Parent Database.

4.2.8 The structure of a Cochrane Systematic Review

Each review incorporated in the database consists of:

- a 'cover sheet', giving the title and citation details of the review; the names of the reviewers; the address and other contact details of the primary reviewer, and the editorial team responsible for the collaborative review group to which the reviewers(s) belong(s); and the sources of support for preparing and updating the review
- an abstract
- a structured report of the review, consisting of an Introduction/statement of objectives; information about the Materials and Methods used; the Results of the systematic review; and a Discussion section
- discussion of the results of the analysis judgements about the implications for practice and research
- full citations of reports of the studies incorporated in the review, and of reports of those studies that were potentially eligible, but which the reviewers(s) decided to exclude (giving reasons for the exclusions)
- tables of the characteristics of the studies included in the review, including information relevant to the assessment of the methodological quality of each of the studies included tables of the results of the review, with presentation of

the statistical syntheses (as Meta-analyses), when these were both possible and appropriate (Mulrow and Oxman 1997:Section 2).

4.2.9 The Cochrane Library

The Cochrane Library distributed on CD-ROM, disk, and available on the Internet, provides rapid access to high quality information about the effects of health care. The main databases are:

4.2.9.1 The Cochrane Database of Systematic Reviews (CDSR) - is a full text database containing systematic reviews of mainly randomised controlled trials. The reviews are in a highly structured format, and evidence is included or excluded on the basis of explicit quality criteria to minimise bias. When appropriate, meta-analysis is used to combine the findings of individual studies to provide an overall estimate of effectiveness. The reviews in CDSR are regularly updated as new information becomes available and in response to comments and criticism and no one has exclusive copyright to the reviews. There are obvious advantages in using electronic media for disseminating and interrogating its contents, making corrections, adding new information etc.

4.2.9.2 The Database of Abstracts of Reviews of Effectiveness (DARE) – contains structured abstracts of good quality systematic reviews from around the world, all of which have been critically appraised by reviewers at the NHS Centre for Reviews and Dissemination at the University of York, England.

4.2.9.3 The Cochrane Controlled Trials Register (CCTR) – contains a bibliography of clinical trials identified by contributors to the Cochrane Collaboration and others, as part of an international effort to hand search the world's journals and create an unbiased source of data for systematic reviews. Other contributors to this database include Medline and Embase, because it has been shown that existing bibliographic databases are inadequate for the identification of all relevant studies.

4.2.9.4 The Cochrane Review Methodology Database (CRMD) – contains a bibliography of books and articles on the science of research synthesis, about the Cochrane Collaboration, contact details and other information on groups in the Cochrane Collaboration. Other Sources of Information include “Netting the Evidence”, where to find information on using evidence in practice on the Internet.

4.2.9.5 Other information – includes **The Cochrane Handbook** on the science of reviewing research; a **glossary** of methodological terms; and **contact details** for review groups and other groupings in the Cochrane Collaboration.

4.2.10 Comments and criticisms

The Cochrane Collaboration considers that efficient arrangements are necessary for criticising the reviews prepared by contributors to the Cochrane Library and for amending reviews in the light of valid criticism. At present, opportunities for criticising reviews before they are published in print are restricted by the number and competence of the referees selected by the editors. After a review has been printed, opportunities for published criticism are usually limited to the few letters that editors can accept for publication, which are often unhelpfully brief and non-specific. It is also frustrating that there is no straightforward way in which the authors of printed reviews can amend their reports after taking account of valid criticism. The quality of a Cochrane Review is being enhanced by means of an iterative system through which successive versions of each review will reflect not only the emergence of new data, but also valid criticisms, solicited or unsolicited, from whatever source. Successive versions of a particular review, together with any intervening criticisms, will be archived electronically. The second and subsequent issues of The Cochrane Library (1997) introduced a new system for submitting comments and criticisms on Cochrane Reviews and protocols. This system consists of a series of screens for entering the comments/criticisms in a highly structured form, followed by options for either transmitting the comments via the Internet, or printing them to be sent by fax or regular mail. The Cochrane Collaboration gladly accepts comments on protocols, as well as reviews, because these can reveal weaknesses at a time when correc-

tions can be made more easily. Comments on protocols provide a form of pre-publication review, while comments on Cochrane Reviews provide for ongoing post-publication review. Future issues of the Database will display summaries of the feedback received for each review in a new section 'View Comments and Criticism' (to be listed just after the 'Conclusions' section). The authors of the review will respond to the feedback sent by users to their reviews in a well-considered and timely fashion. The authors' responses will be displayed along with the comments, and the names of those submitting criticism will be acknowledged.

4.2.11 Making good decisions about health care

Making good decisions about health care rely on more than good reviews of the results of research. The Cochrane Collaboration seeks to make the results of research assessing the effects of health care more easily available but if better decisions are to lead to improved health, then effective mechanisms are needed for implementing them. Forms of care that have been shown to do more good than harm should be encouraged, while those that do more harm than good need to be discarded. The many forms of care which have unknown effects should, as far as possible, be used in the context of a research programme to find out whether they help or do harm. In addition, policy makers and decision-makers must consider people's needs, the availability of resources, and priorities. In making decisions about the care of individual patients, the results of the reviews must also be integrated with the clinician's expertise, which has been acquired through experience and practice. The results of the reviews must also be integrated with the patients expertise, which derives from their knowledge of their condition (particularly if it is a chronic or recurrent health problem), the treatment on offer, and the responsiveness or otherwise of the former to the latter. Finally, the findings in a systematic review of research evidence may, very rarely, appear to have universally relevant implications. Usually, however, universal guidelines and prescriptions for the precise application of the evidence are neither wise nor workable. Local disease burdens and barriers to implementation vary widely from country to country and from place to place within countries,

and local attention to these issues will help to ensure that the evidence will help those who can best benefit from it.

4.2.12 Strategic alliances and the future

Many of the achievements of the Cochrane Collaboration reflect the goodwill and efforts of the individuals who have contributed and continue to contribute their time and effort to the Collaboration's activities. However, within the Cochrane Collaboration an elected steering group now governs the conduct and evolution of the Collaboration and has recently prepared a strategic plan for the future at local, national and global levels. (Sections 4.2.1-4.2.12 are summaries of the Cochrane Collaboration Information Booklet (1997))

4.2.13 Conclusions

This section is a review of the main areas covered by the Cochrane Collaboration Handbook (Mulrow CD, Oxman AD (eds.) (1997)) and the Cochrane Collaboration Information Booklet (1997) in order to provide the remaining background information for the rest of the thesis and may be summarised as follows:

1. The Cochrane Collaboration is an international organisation that aims to help people make well-informed decisions about healthcare by preparing, maintaining and promoting the accessibility of systematic reviews of the effects of healthcare interventions.
2. Cochrane Reviews are systematic, up-to-date summaries of reliable evidence of the benefits and risks of healthcare intended to help people make practical decisions and are published electronically in successive issues of *The Cochrane Database of Systematic Reviews*.
3. Preparation and maintenance of Cochrane Reviews is the responsibility of international collaborative review groups and in the case of this research study being the Cochrane Musculoskeletal Group (CMSG)- Back Subgroup based in the Institute for Work and Health, Toronto, Canada.

4. Cochrane Systematic Reviews are in a highly structured format, and evidence is included or excluded on the basis of explicit quality criteria in order to minimise bias.
5. When appropriate, meta-analysis is used to combine the findings of individual studies to provide an overall estimate of effectiveness.
6. The reviews in CDSR are regularly updated as new information becomes available and in response to comments and criticism
7. No one person or organisation has exclusive copyright to the reviews

The following sections of this thesis (4.3-4-7) closely follows the Cochrane Collaboration guidelines for:

- Developing the research protocol and formulating the problem (4.3)
- Developing the Cochrane Review; locating and selecting studies, critical appraisal of studies, collecting data, analysing and presenting results, and interpreting results (4.4)
- Developing the Review for inclusion in The Cochrane Library (4.5)
- Developing the Review by improvement and updating through the Cochrane Comments and Criticism mechanism (4.6)
- Developing appropriate conclusions and recommendations based on this review (4.7).

The next section of this thesis (4.3) follows the Cochrane Collaboration guidelines for developing the research protocol and formulating the problem.

4.3 Developing a Protocol for a Cochrane Systematic Review

This section of the thesis is structured on, extracted from, and is a summary of, the following sections from the Cochrane Collaboration Handbook: the 'Introduction', 'Formulating the Problem', and 'Developing a Protocol' (Oxman 1994). Supplementary material, using a case study approach, follows each main subsection summarised from the Cochrane Collaboration Handbook, in the form of an application commentary, outlining the authors' use of these guidelines in the construction of the Cochrane Review Protocol.

4.3.1 Introduction

Healthcare providers, consumers, researchers, and policy makers are inundated with unmanageable amounts of information and systematic reviews are needed to efficiently integrate valid information and provide a basis for rational decision making. Systematic reviews establish where the effects of healthcare are consistent and research results can be applied across populations, settings, and differences in treatment (e.g. dose or electrical parameters); and where effects may vary significantly. The use of explicit, systematic methods in reviews limits bias (systematic errors) and reduces random errors (simple mistakes), thus providing more reliable results upon which to draw conclusions and make decisions. Meta-analysis, the use of statistical methods to summarise the results of independent studies, can provide more precise estimates of the effects of healthcare than those derived from the individual studies included in a review.

The aim of the Cochrane Collaboration and its Handbook is to help reviewers make good decisions about the methods they use relative to the specific healthcare problems that they address, rather than dictate arbitrary standards. The Cochrane Collaboration and the Handbook focus particularly on systematic reviews of randomised controlled

trials (RCT's) because they are likely to provide more reliable information than other sources of evidence on the differential effects of alternative forms of healthcare at this time. The basic principles of reviewing research are the same, whatever type of evidence is being reviewed. Although they focus mainly on systematic reviews of RCT's they address issues specific to reviewing other types of evidence when this is relevant.

Cochrane Reviews have a standard format and those preparing a review begin by developing a protocol. The seven steps of preparing and maintaining a systematic review are:

- 1. Formulating the problem*
- 2. Locating and selecting studies*
- 3. Critical appraisal of studies*
- 4. Collecting data*
- 5. Analysing and presenting results*
- 6. Interpreting results*
- 7. Improving and updating reviews.*

(Oxman 1994)

4.3.1.1 Commentary: This introduction describes the bases for systematic reviews and meta-analysis of randomised controlled trials, originating from The Cochrane Collaboration Handbook (1997), albeit, the original 1994 version was used as the foundation for the author's own systematic review protocol which is shown in full at the end of this section.

An application to join the Cochrane collaboration was made on the 25th November 1994 and discussions concerning the most appropriate group to join continued until the end of May 1995, when the author was eventually allocated to the Back Subgroup of the Cochrane Musculo-skeletal Group(CMSG).

4.3.2 Formulating the problem

The first and most important decision in preparing a review is to determine its focus by asking clearly framed questions. Such questions guide the review process including strategies for locating and selecting studies or data, for critically appraising their relevance and validity, and for analysing variation among their results. In addition, readers in their initial assessments of relevance use a review's questions and objectives. A clearly defined question should specify the types of participants, interventions or exposures, outcomes of interest and the types of studies that are relevant to answering the question. The more precise the review is in defining components, the more focused the review. Reviewers also need to understand the terms and language used in various countries to describe these components.

It is helpful to consider the types of people we are interested in and to define the disease or condition that are of interest using explicit criteria for establishing its presence and then identify the population and setting of interest. Any restrictions with respect to specific population characteristics or settings should be based on solid ground. When there is uncertainty about important differences in effects among different subgroups it is probably best to include all of the relevant subgroups and then test for important differences in effect in the analysis. We need to specify the types of interventions that are of interest and to define the types of control groups that are acceptable and whether persons in a control group might receive interventions other than a placebo and if those interventions overlap with the active intervention. We also need to delineate the outcomes of interest as Cochrane Reviews should include all reported outcomes that are likely to be meaningful to people making a decision about the healthcare problem the review addresses. It may be possible to acquire unpublished data from investigators in order to disentangle combined outcomes.

Cochrane Reviews focus primarily on randomised controlled trials as they are considered by many to be the gold standard for assessing

therapeutic efficacy at this moment in time. Other aspects relevant to study design which require consideration are whether to review studies that have a placebo comparison group, that evaluate outcomes in an unbiased manner, or have a certain length of follow-up. Reviewers should be cautious about including non-randomised studies in a review. Although it is possible to control for confounders that are known and measured using other study designs, randomisation is the only way to control for confounders that are not known or not measured. Empirical evidence suggests that, on average, non-randomised studies tend to overestimate the effects of health care. It is often difficult to locate RCT's and there is also a risk of publication bias. Trials that do not show an intervention to be effective are sometimes less likely to be published than trials that show an effect. This means that systematic reviews that fail to include unpublished trials may be biased towards overestimating the effectiveness of an intervention. Extensive efforts are going into building registers of controlled trials to make it easier for reviewers to locate randomised controlled trials. It may sometimes be appropriate to conduct a systematic review of non-randomised studies of the effects of healthcare.

Once a well-formulated question has been prepared, it is then necessary to determine which key components to focus on in initial searching strategies and the search for studies is greatly facilitated by the availability of trial registers. Formulating a question in terms of the types of participants, interventions, outcomes and study designs of interest will lead naturally to specifying the criteria that will be used to select studies. Details relevant to key components of questions are what reviewers collect from individual studies and determine the final criteria that will be used to select appropriate studies for review and what data should be abstracted from studies meeting those selection criteria.

The questions that a review addresses may be broad or narrow in scope. Narrowly focused reviews may not be generalisable to multiple settings, populations, and formulations of an intervention and they can also result in spurious or biased conclusions in the same way that sub-

group analyses sometimes do. On the other hand a narrow focus is at high risk of resulting in biased conclusions, when the reviewer is familiar with the literature in an area and narrows the inclusion criteria in such a way that one or more studies with results that are in conflict with the reviewer's beliefs are excluded. Searches for data relevant to broad questions may also be more time-consuming and more expensive than searches relevant to narrowly defined questions. As broad questions may be addressed by large sets of heterogeneous studies, synthesis and interpretation of data may also be particularly challenging.

Systematic Reviews are analyses of existing data that are constrained by previously chosen study populations, settings, intervention formulations, outcome measures and study designs. However, it is generally not possible to formulate an answerable question for a review without knowing some of the studies relevant to the question, and it may become clear that the questions a review addresses need to be modified in light of evidence accumulated in the process of conducting the review. Although a certain fluidity and refinement of questions is to be expected in reviews as one gains a fuller understanding of the problem, it is important to guard against bias in modifying questions e.g. post-hoc questions are more susceptible to bias than those asked a priori, and data-driven questions can generate false conclusions based on spurious results. (Oxman 1994)

4.3.2.1 Commentary: The protocol stage of this Cochrane review was constructed following the above guidelines to formulate the problem and to determine its focus. A comparison between the protocol objectives and the review objectives show a clear progression from a simple statement of intent i.e. to determine the effectiveness and safety of transcutaneous electrical nerve stimulation on patients with a history of chronic low back pain, with the outcomes of interest described for pain relief and physical activity, to a highly structured set of ten hypotheses (see the Cochrane Review section 4.4 and 4.5).

It soon became clear as the research progressed that in order to

meet the focus of the basic questions a more structured set of hypotheses was necessary and these are described in full in the completed review.

The criteria for considering studies for this review also underwent further development, as the research questions became more precise and the components more defined. The types of studies for this review was determined as all randomised controlled trials of Transcutaneous Electrical Nerve Stimulation (TENS) and Acupuncture-Like Transcutaneous Electrical Nerve Stimulation (ALTENS) versus a placebo control in the rehabilitation of patients with chronic low back pain of more than 8 weeks duration.

The types of participants remained unchanged.

The types of intervention became more defined from 'the electrotherapy techniques of TENS/ALTENS' to a more clearly defined set of TENS/ALTENS treatments with specific electrical parameters versus a credible placebo control rather than another active treatment comparison such as massage or ice therapy.

The types of outcome measures considered in the review also developed from the two general outcomes described in the protocol to a highly structured set of six outcome measures as described in the full review.

This Cochrane Review focuses primarily on randomised placebo controlled trials as they are considered by many to be the 'gold standard' for assessing therapeutic efficacy at this time. However, all the studies, controlled and uncontrolled, identified through the search strategy described in the next section were collected and assessed by the team of assessors for study quality and those not meeting the inclusion criteria were also assessed and then used to support the main findings from the randomised controlled trials.

The key components of the studies and data collection were identified and are described in the section dealing with the search strategies. The search for studies for this review was not facilitated by the availability of a trial register although one is now being developed by

the Back subgroup of the Musculoskeletal Group (CMSG) of the Cochrane Collaboration.

The questions that this review addresses are narrow in scope, focussing on conventional and acupuncture-like TENS and excluding other peripheral therapies not meeting the accepted electrical parameters of the above, e.g. subliminal applications and novel techniques e.g. mixing TENS and ALTENS and other electrical parameters. These modifications became necessary in the light of evidence accumulated early in the process of conducting this review in order that we are able to compare like-with-like in the final analysis.

4.3.3 Developing a Protocol

Preparing a review is a complex process that comprises many judgements and as in any scientific endeavour, the methods to be used are established beforehand. Since systematic reviews are retrospective analyses of data collected by others, it is important to make the process as rigorous and well defined as possible. However, just as protocols for Randomised Controlled Trials must sometimes be changed to adapt to unanticipated circumstances changes in a review protocol are sometimes necessary but changes in the protocol should not be made on the basis of the results. Post hoc decisions (such as excluding selected studies) that are made when the impact on the results of the review is known are highly susceptible to bias and should be avoided.

The protocol for a Cochrane Review should consist of drafts of the appropriate sections of the final report (see also 4.4.1) as:

1. Cover sheet
2. Background
3. Objectives
4. Selection criteria
5. Search strategy
6. Methods

The protocol begins with a brief synthesis of the underlying biology, psychology or sociology and healthcare issues that provide the motivation and rationale for the review. Systematic reviews can be conducted in an effort to resolve conflicting evidence, to answer questions where the answer is uncertain or to explain variations in practice. They are intended first and foremost to provide unbiased, up-to-date summaries of what we know and do not know about the effects of different forms of healthcare.

Reviews should address outcomes that are meaningful to people making decisions about healthcare and it is not helpful to include in a review evidence where the risk of bias is high, even if there is no better evidence. The primary aim of a Cochrane Review should be to summarise and help people to understand the evidence. The background and questions (objectives) along with the proposed search strategy and plans for collecting and analysing data form the basis of the protocol of a Cochrane Review and editors of Collaborative Review Groups appraise and give feedback on these protocols before actual reviews are conducted (Oxman 1994)

4.3.3.1 Commentary: The following protocol for the review on 'The effectiveness of TENS and ALTENS in chronic low back pain' was constructed in accordance with the basic guidelines in operation at the time (1994/5) of its creation. This review was conducted in an effort to resolve conflicting evidence surrounding the use of TENS and ALTENS for chronic low back pain, to attempt to answer these questions. even though the answers may still remain somewhat uncertain even now, and to explain variations in practice, especially those related to treatment frequencies, electrode placements, length of treatment and patient suitability. The protocol was submitted to the Back Subgroup of the Cochrane Collaboration on the 13th May 1995. This protocol was reviewed and approved "without further changes" by the editorial team of the Back Subgroup of the Cochrane Collaboration Musculoskeletal Group on November 21st 1995.

4.3.4 The Research Protocol for assessing the effectiveness of TENS and ALTENS in chronic low back pain {extracted from the Cochrane Library and RevMan into thesis format}:

Title: The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain.

Background: The practitioner specialising in musculo-skeletal diseases is fully aware that the most common complaint worldwide is chronic low-back pain. The frequency of this complaint stands in contrast to the significant lack of understanding of its effective treatment and prognosis (Mooney and Cairns 1978) and attempts to decrease its impact by different educational, ergonomic, or treatment methods have generally failed (Nachemson 1983). The diagnosis of lumbar pain syndromes remains a difficult conundrum. Pain syndromes are given many names in an attempt to describe what is probably most appropriately non-specific lumbar pain with and without radicular referral. The name used reflects the background, training, speciality and bias of the examiner. Some commonly used terms include lumbar sprain, lumbar strain, lumbago, myofascial pain, ilio-lumbar ligament syndrome, sacro-iliac dysfunction, lumbar misalignment and multifidus syndrome (Saal and Saal 1991).

In the UK, for example, 1 in 5 people will suffer from low-back pain during their lifetimes. By 1991, the number of working days lost per year had risen to 57 million days at an estimated cost of £2 billion (Breen 1993). In the United States low-back pain, often of a chronic nature, results in expenditure of \$13 billion a year for medical care (Deyo 1990). Early rehabilitation and a prompt return to work is important for stemming the staggering economic drain that results from chronic disability. The development of cost-effective strategies for returning the patient to optimal levels of functioning as rapidly as possible has remained a therapeutic challenge (Herman 1994). A number

of simultaneous treatments are usually advocated for patients with chronic pain, but few of these treatments have ever been subjected to rigorous clinical evaluation. Transcutaneous electrical nerve stimulation (TENS), originally based on the gate-control theory of pain (Melzack and Wall 1965) is widely used for back pain but despite its wide use and theoretical rationale there is meagre scientific evidence at this stage to support its use, this based on the controlled trials of the efficacy of TENS in treating chronic back pain up to 1990 (Deyo et al 1990).

Transcutaneous electrical nerve stimulation (TENS) is also known as conventional high frequency, low intensity TENS and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) is also known as low frequency, high intensity TENS. Transcutaneous electrical nerve stimulation (TENS) is based on the gate-control theory of pain using frequencies of stimulation above 10Hz but usually between 80-100Hz. Acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) is based on the mode of traditional acupuncture needle stimulation which is usually less than 3 pulses per second and the presumed working mechanism of the endorphin response and these two modalities for chronic low-back pain management have experienced a tremendous growth over the past 25 years. The publication of the gate-control mechanism (Melzack and Wall 1965) also seems to be responsible for the proliferation of electric devices and applications of TENS and ALTENS within all areas of pain control not only that of chronic back-pain management. The literature both positive and negative has been subjected to extensive narrative reviews (Shealy 1974; Long 1991; Shealy and Mauldin 1994) and it was suggested more than 20 years ago that TENS had a phenomenally important role to play in acute and chronic pain management, which has scarcely been recognised, and that large numbers of pain patients should benefit from this approach (Shealy 1974). There has been many trials of TENS and ALTENS since then with over 600 publications (Nolan 1991) supporting its efficacy with up to 80 % in acute

back pain problems and at least 50% in chronic back pain (Shealy 1994). However, there have been other studies (e.g. Deyo 1990) which have refuted this effectiveness.

In view of these claims and counterclaims it would now seem appropriate to prepare and maintain a systematic review (see Chalmers and Altman 1995) within the framework of the Cochrane Collaboration methodology in order to evaluate the claims more rigorously. If TENS and ALTENS, are proved to be therapeutically effective and cost-effective using the Cochrane Collaboration systematic review techniques, then the potential scale of their use world-wide would be enormous.

Objective: The objective of this review is to determine the effectiveness and safety of transcutaneous electrical nerve stimulation (TENS and ALTENS) treatments carried out on patients with a history of chronic low-back pain of 8 weeks duration or longer over the last 20 years. The main outcomes of interest are:

1. a substantial improvement in pain levels as measured by an appropriately validated clinical pain intensity rating method such as the (Revised) Oswestry Low Back Pain Questionnaire; the McGill Pain Questionnaire; or a Visual Analogue Scale (VAS), a Numerical Rating Scale (NRS), a Box Scale (BS), a Behavioural Rating Scale (BRS), or a Verbal Rating Scale (VRS) after Jensen (1986) and/or
2. an improved level of physical activity as determined by a suitably validated activity scale such as the Roland-Morris Activity Scale or a patient self- assessment or by an examiner assessment in respect of the following outcomes:-
 - a. an improvement would be recorded if a total or partial relief of pain was experienced.
 - b. a non-improvement would be recorded if no decrease in pain rating occurred at the end of the course of treatment.
 - c. an improvement in physical activity levels would be recorded if a total or partial return to normal functioning occurred

and/or there was a full or partial return to work experienced either subjectively by the patient or objectively by a practitioner examination.

d. a non-improvement would be recorded if no change in the level of physical activity at the end of the course of treatment was experienced.

Among patients with chronic low-back pain of 8 weeks duration or longer, we wish to test the following:

1. TENS treatment for chronic low-back pain reduces pain and/or increases physical activity without any significant side-effects.
2. ALTENS treatment for chronic low-back pain reduces pain and/or increases physical activity without any significant side effects.
3. The efficacy of TENS and ALTENS will be compared.

Criteria for considering trials for this review:

We seek to identify all randomised, controlled trials in which TENS or ALTENS has been used in comparison with a control or standard treatment in the rehabilitation of patients with chronic low-back pain of at least 8 weeks duration over the last 20 years.

Types of participants:

Trials of TENS or ALTENS treatment with randomised patients of either gender with chronic low-back pain, irrespective of the specific local diagnosis, and with a history of at least 8 weeks duration.

Types of intervention:

The electrotherapy techniques of TENS or ALTENS.

Types of outcome measures:

The main outcomes of interest are:

- (1). the percentages of patients with chronic low-back pain who after a course of treatment had less pain as measured by an appropriate rating scale and/or greater physical activity as measured by the pa-

tient or examiner in the test or control groups and

(2). whether the effectiveness of TENS differs from that of ALTENS.

Search strategy for identification of trials:

1. Relevant randomised trials are being identified by regular monthly searches of the Medline CD ROM facility at De Montfort University.
2. Searches of the CISCOR and AMED databases have already been conducted.
3. Additional search sources include the reference lists of trials and narrative review articles.
4. Searching books related to physical therapies and acupuncture/electroacupuncture techniques.
5. Searching published abstracts from pain conferences.
6. Conversation with colleagues (particularly those who have coordinated such studies and those who have their own database of trials).
7. Sending letters to major investigators of TENS and ALTENS techniques seeking information on published and unpublished trials.
8. Searching the international register of RCT's via the US National Library of Medicine's Medline database when it comes on-line.
9. A search application will be made to the Baltimore Cochrane Centre holding the Master List of Journals being searched by hand.

Methods of the review (after Oxman 1994):

The target date for completion of this review is August 31st. 1996.

Methods used to select trials for inclusion: the inclusion criteria will be liberally applied in deciding which articles to retrieve. Three reviewers (JGG, AB, MWF), all content area experts, will independently evaluate the trials to be included in the review. The names of the authors, institutions, journal of publication and results will be made known to the reviewers. The decision rule for disagreements will be resolved by discussion or by a majority decision 2:1. A pilot examination to test the inclusion criteria will be carried out on three studies to re-

fine and clarify the research tools.

The criteria and methods used to assess the methodological quality of the included trials: will be assessed by the same three reviewers (JGG, AB, MWF).

We have decided to assess the main criterion for quality on an alphabetical scale A-C:-

A criterion met, C criterion not met and B criterion partially met or it is unclear whether the criterion was met. The following criteria of quality will be assessed using the above methodology:

1. A main criteria of quality is adequate allocation concealment:

All trials will be judged on the reported method by which allocation was concealed using the following A-C scale:

A = adequate concealment: some form of centralised, randomisation scheme via office by phone to receive the treatment allocation; an on-site computer system with access only after inputting the characteristics of an enrolled participant; by assignment envelopes, sequentially numbered, sealed and opaque; other methods that ensure adequate concealment.

C = inadequate concealment: alternation; reference to case record numbers, dates of birth, day of the week or similar approach; any allocation procedure that is entirely transparent before assignment, such as an open list of random numbers.

B = unclear concealment: stating that a list or table was used for assignment; just specifying that envelopes or, sealed envelopes were used; any other unclear allocation scheme.

2. Other components of trial quality to be considered in this review:

a) Double-blinding: was the study described as double-blind, bearing in mind the perennial problem of how double-blind can a physical treatment be?

b) Control/ placebo intervention: were the physical characteristics of the control/ placebo intervention credible?

c) Pain and/or activity assessments: were the assessment techniques

valid e.g. a validated pain or activity assessment method. Was the level of activity assessed subjectively or objectively?

The quality of all the trials that meet the inclusion criteria will be assessed in accordance with the explicit criteria identified above under methods used to select trials for inclusion. The quality assessments so determined will then be used as weighting in the final statistical analysis and will be identified on the Characteristics of Trials Contributing to the Review data sheet.

The methods used to collect data from the included trials:

Data regarding the study populations, interventions, outcome and quality measures, and the results will be independently extracted by the three reviewers (JGG, AB, MWF) using the Reviewers Check List and the Characteristics of Trials Contributing to the Review sheet. Data on the number with each outcome event, by allocated treated group, irrespective of compliance, and whether or not the patient was deemed ineligible or otherwise excluded from treatment or follow-up will be sought to allow an intention-to-treat analysis. If any of the above information is not available in the publications, it will be sought by correspondence with the trial authors.

Characteristics of the included trials:

Key characteristics of the trials will be recorded on the Characteristics of Trials Contributing Data to the Review data sheet and will include: the trial reference name and year; the methodological quality; characteristics of the participants; characteristics of the interventions (comparison groups), characteristics of the outcome measures, and important notes.

Results of the included trials:

The summary results of the included trials will be extracted to the Reviewers Check List data sheets and will include: Reviewer details, trial identification, types of participants, types of intervention,

types of outcomes results for pain and activity levels, and methodological quality for the two subgroups of TENS and ALTENS.

Methods used to synthesise the data:

The systematic review and meta-analysis will be made on the database of studies comprising randomized and non-randomized studies, blind and unblind studies and studies of varying power but subsidiary analyses would restrict attention to randomized or blind or powerful studies to investigate the impact of these measures of study quality:

1. Choice of summary statistic: the initial analysis (if the material allows) of binary outcomes will employ the odds ratio (OR) using the log odds Peto method (APT 1994) and the relative risk (RR) statistic using the Review Manager software.
2. Test for heterogeneity: to check whether the differences among the results of the trials are greater than could be expected by chance using an analysis of a graphical display of the results and/or automatic testing by the Review Manager software.
3. Estimate of overall effect: A weighted average of the results of all the available required quality trials will be made. The weight given to each trial will be determined by the quality of the study together with the more precise estimates from larger studies with more events. A fixed effects model will be used to test significance for the overall null hypothesis (no effect in all trials) and an estimate of the average overall treatment effect. The confidence interval for that effect will then be calculated using the Review Manager software.
4. Sensitivity analyses: test of the sensitivity of the results will be determined with respect to changes in the inclusion criteria, trial exclusion where there was some ambiguity of the inclusion criteria and whether there was exclusion of studies of lower methodological quality or requiring data re-analysis.
5. Subgroup analyses: the review will compare the two subgroups of TENS and ALTENS for efficacy.

4.3.5 Conclusion

This protocol was constructed in accordance with the guidelines of the Cochrane Collaboration Handbook, in operation at the time of its creation (1994/5), and served as the research document for the preparation of the Cochrane Review on “The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with low back pain”.

The following section (4.4) of the thesis examines the Cochrane Collaboration Handbook Guidelines, together with the author's commentary, for constructing the systematic review and meta-analysis and their implementation in the tertiary research process under examination.

4.4 Developing A Cochrane Systematic Review

This section of the thesis is also structured on, extracted from, and is a summary of, the following sections from the Cochrane Collaboration Handbook: 'Format of a Cochrane review', 'Locating and selecting studies', 'Critical appraisal of studies', 'Collecting data', 'Analysing and presenting results', and 'Interpreting results', (Mulrow and Oxman 1997-b/e/f/g/h/i). Supplementary material, again using a case study approach, follows each main subsection summarised from the Cochrane Collaboration Handbook, in the form of an application commentary outlining the authors' use of these guidelines in the construction of the Cochrane Review under consideration in this thesis.

4.4.1 Format of a Cochrane Review

The format of a Cochrane Review has several objectives. It helps readers to find the results of research quickly and to assess the validity, applicability, and implications of those results. It guides reviewers to report their work explicitly and concisely, and minimises the effort required to do this. This format is also suited to electronic publication and updating, and it generates reports that are informative and readable when viewed on a computer monitor or printed. The Cochrane Collaboration 'RevMan' software is designed to help reviewers in constructing reviews in the appropriate format and to prepare files required to transfer reviews electronically to *The Cochrane Database of Systematic Reviews* (CDSR). Standard headings and tables guide reviewers preparing a report and make it easier for readers to identify information that is of particular interest to them as shown below.

4.4.1.1 Outline of a Cochrane Review

Cover sheet:

Title

Short title

Reviewer(s)

Contact address

Name

Organisation and address

Telephone number

Facsimile number

E-mail

Date last edited

Date of last substantive update

Sources of support to the review

Abstract

Objectives

Search strategy

Selection criteria

Data collection & analysis

Main results

Conclusions

Text

Background

Objectives

Selection criteria

Types of studies

Types of participants

Types of interventions

Types of outcome measures

Search strategy

Methods

Description of studies

Methodological quality

Results

Discussion

Conclusions

Implications for practice

Implications for research

Acknowledgements

Conflicts of interest

Tables and figures:

Table of comparisons

Table of included studies

Table of excluded studies

Data tables and graphs

References:

References to studies

Studies included in this review

Studies excluded from this review

Studies awaiting assessment

Ongoing studies

Other references

Additional references

Previously published versions of this review

Table XVI Outline of a Cochrane Review (Mulrow and Oxman 1997b)

4.4.1.2 Commentary: The author's Cochrane Review (4.5) follows the above format and was entered into the RevMan software following a Training Workshop on 'Getting a review into RevMan' held by the UK Cochrane Centre, Oxford University Computing Centre, on Thursday 30th May 1996. This review was submitted to the editorial committee of the Back subgroup of the Cochrane Collaboration Musculoskeletal Group (CMSG) on the 19th August 1996. Three editors from the Back subgroup read and evaluated the review and their comments were re-

ceived on the 20th September 1996. The systematic review was revised in the light of the editorial comments, albeit some of these editorial comments and suggestions were challenged as being incorrect, and the review was resubmitted on the 25th November 1996 and accepted for publication in the Cochrane Library on the 2nd December 1996. This review became the first completed Cochrane Review in the CMSG Back Subgroup, and remained the only one at the time of thesis completion (January 1998), and was subsequently published in The Cochrane Library on CD-ROM, Issue 1, February 1997 (and subsequent issues). This Cochrane Systematic Review on "The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain" and citation details are presented in full in the next section of the thesis.

4.4.2. Locating and selecting studies

A comprehensive, unbiased search is one of the key differences between a systematic review and a traditional review. While electronic databases such as MEDLINE are powerful tools for locating studies, only 30 - 80% of all known published randomised controlled trials are identifiable using MEDLINE. Non-English-language references are under-represented in MEDLINE and only published articles are included. To protect against bias and ensure that all relevant data are included in a review it is important to use multiple sources to identify studies and a systematic approach to selecting studies.

The primary source of studies for Cochrane Reviews is a review group's trial's register and the approach that is used should be reported in the review. Reviewers should check the reference lists of all relevant articles that are obtained as this is generally an efficient means of identifying studies. Additional, potentially relevant, articles that are identified should be retrieved and assessed for possible inclusion in the review. The potential for reference bias (a tendency to preferentially cite

studies supporting one's own views) when doing this should be kept in mind and guarded against. Existing reviews should be obtained and checked for references to the original studies. The Cochrane Library also includes the York Database of Abstracts of Reviews of Effectiveness (DARE) which provides information on previously published reviews of the effects of healthcare and should also be checked. MEDLINE, EMBASE, and other bibliographic databases can also be used to identify review articles. Colleagues can be an important source of information on recent trials that have not yet been published or on older trials, which were never published.

Electronic Databases are the second important source for identifying trials. The Cochrane Controlled Trials Register (CCTR) is part of the Cochrane Library and contains reference information to randomised controlled trials and controlled clinical trials in health care. Index Medicus and Excerpta Medica are indexes of healthcare journals that are available in electronic form as MEDLINE and EMBASE, respectively. Studies comparing searches of the two databases have generally concluded that a comprehensive search requires that both databases be searched. Science Citation Index, and its electronic counterpart Scisearch, lists where a published article was subsequently cited. Registers containing references to planned, ongoing or completed trials, which were registered prospectively, can also be a valuable source of trials. Occasionally other bibliographic databases may provide a useful additional source for identifying trials for a specific review. Finally, to facilitate the location of all published trials the Cochrane Collaboration has organised extensive hand searching efforts; i.e. manually examining each issue of a journal and reading each title/abstract/body of an article sufficiently to determine whether the article is a randomised controlled trial (RCT), a controlled clinical trial (CCT) or a meta-analysis.

The process by which studies will be selected for inclusion in a review should be described in the protocol. The selection of studies for inclusion in a review is a funnelling process that involves multiple stages. When reviewing the results of an electronic search, the first

stage involves assessing titles and abstracts to determine whether each article might meet predetermined eligibility criteria. Review of the full text may lead the reviewer to exclude the study because it does not meet inclusion criteria. At each stage of the selection process it is important to err on the side of over-inclusion because once a trial has been excluded from the selection process it is unlikely to be reconsidered. Librarians who have specialised in electronic searching can often be helpful in developing and executing a search strategy and it is important to work closely with a librarian in deciding which databases to search and what search terms to use in each database. The UK Cochrane Centre has designed a search strategy for RCT's that includes controlled-vocabulary and free text terms such as "randomized-controlled-trial," "clinical trial" and "placebo".

All the articles that are identified must then be assessed to see whether the inclusion criteria for the review have been met and:

1. whether more than one reviewer will assess the relevance of each article
2. whether the decisions concerning relevance will be made by content area experts, non-experts, or both
3. whether the people assessing the relevance of studies will know the names of the authors, institutions, journal of publication and results when they apply the inclusion criteria
4. and how disagreements will be handled if more than one reviewer applies the criteria to each article

The number of people assessing the relevance of each trial should be stated in the Methods section of the review. Experts in a particular area may have pre-formed opinions that can bias their assessments of both the relevance and validity of articles. Some reviewers may decide that assessments of relevance should be made by people who are blind to the journal from which the article comes, the authors, the institution, and the magnitude and direction of the results by editing copies of the articles. Disagreements about whether a trial should be included can generally be resolved by discussion or by consensus. For most reviews

it will be worthwhile to pilot test the inclusion criteria on a sample of articles and to refine and clarify the inclusion criteria, train the people who will be applying them and ensure that the criteria can be applied consistently by more than one person.

The search strategy should be described in sufficient detail that the process could be replicated. Documentation of the search strategy should include the main sources that were used to locate studies, the search strategy for each database that was searched; temporal constraints (e.g. 1966 to 1996); language constraints; and how and when the review group's trials register was last checked. Because Cochrane Reviews are kept up-to-date, searches are ongoing and both the search strategies that are used and the reporting of these strategies can continue to be improved

A reference management system eases the work of identifying duplicate titles and also assists in tracking the retrieval status of each article. It is also a good idea to document the reason for exclusion of each article that was identified but ultimately not included in the review. When searching multiple databases it can be helpful to know which references were identified in each database. This can help guide decisions about which databases to search routinely for maintaining the review group's trials register and, if appropriate, individual reviews.

It is important that efforts to develop and maintain trials registers are co-ordinated effectively and efficiently in order to maximise access to studies by reviewers, thereby helping to ensure that reviews are comprehensive, up-to-date and unbiased (Mulrow and Oxman 1997e)

4.4.2.1 Commentary: The methodology for locating and selecting studies for this review followed the earlier guidelines in the Cochrane Handbook on which the above text is based. The search strategy is described in detail in the review (4.5) and this takes into account that a comprehensive unbiased search is one of the key differences between a systematic review and a traditional literature review.

The search strategy initially limited the studies selected to those

published in the English language because of the lack of available translation resources. However, this subject and the issues surrounding it are covered in some depth in section 4.6 of this thesis under 'Improving and updating systematic reviews using the Cochrane Collaboration Comments and Criticisms Mechanism'.

Whilst the primary source of studies for Cochrane Reviews is held to be the review groups trials register, this was not applicable in this instance due to the non-existence of the register at the time of implementing the search strategy or at the time of completing this thesis. Checking the reference lists of all relevant articles became the most efficient way of identifying additional studies as the York Database of Abstracts of Reviews of Effectiveness was also not available at the time of initial searching. The potential for reference bias was kept in mind and to guard against this a team of three content area specialist reviewers (the author, Dr Michael Flowerdew, and Professor Alan Bennett) was used to initially select the studies for this review. Dr Frank Dewhurst, Mr Philip Jarvis, and Professor Mike Saks of the De Montfort University Departments of Biological Sciences, Medical Statistics and the School of Health and Community Studies provided academic monitoring of the research process respectively

The search strategy of multiple electronic databases, the second most important source for identifying trials is fully described in the protocol and in the Cochrane Review text itself and the process for selecting studies for inclusion is fully described under the 'methods of the review' section in (4.5). In view of the dearth of studies identified under the initial search strategy for electrostimulation (and its variants) and chronic back pain, the search was then widened to include all studies of electrostimulation for pain. This enabled the researcher to identify those studies of electrostimulation for chronic low back pain covered by the second search terms of 'pain' alone and to reject those not relevant to the review. The help of the De Montfort University academic librarians, with specialised skills in electronic searching, is acknowledged here. The UK Cochrane Centre has now designed

a search strategy for RCT's that includes controlled vocabulary and free text term but again this was not available in time for this review.

The initial 68 articles identified were then assessed by the three reviewers to see whether the inclusion criteria had been met. The content area expert reviewers assessed the relevance of each article and they were not blinded to the names of the authors, institutions, journal of publication or when applying the inclusion criteria and any disagreements were resolved by a majority decision of 2:1. Whilst experts in a particular area may have pre-formed opinions that can bias their assessments of both relevance and validity it was felt necessary to seek content area experts for this review, in order to evaluate the finer points of TENS, ALTENS and electrical parameters. A decision which was later validated by the editorial teams' inability to understand some of the finer details of the studies assessments and inclusion and exclusion criteria. This aspect is discussed further in section 4.6. It is now recommended that reviewers should be blinded to the above study characteristics but there were no guidelines on this at the time and we followed (Blair 1995) recommendations not to blind the reviewers, in view of the difficulty recognising that several of the reports were from the same study rather than individual studies. This issue and related recent research is also discussed in more detail in section 4.6

We carried out a pilot test on the inclusion criteria on a sample of three articles using data collection forms (described later - see Appendix B (ii)) in order to refine and clarify the inclusion criteria and to ensure consistency of use by the reviewers.

A reference management system was not used in this review but all studies were entered into a Word 6 for Windows file which could be quickly searched (using the 'find' mode) in order to identify duplicate titles for studies and all other references. The main advantage using this system was that all information was already in Word 6 for windows word processor format to facilitate incorporation into appropriate Cochrane software and thesis software too. Unfortunately there is no

electronic record of which references were identified in which database apart from full hardcopy listings.

4.4.3 Critical appraisal of studies

Critical appraisal of individual studies that are summarised in systematic reviews is necessary to limit bias in conducting the systematic review, gain insight into potential comparisons, and guide interpretation of findings. Parameters that warrant appraisal are those related to applicability of findings, validity of individual studies, and certain design characteristics that affect interpretation of results. Specifically, whether a review's findings are applicable to a particular population, intervention strategy or outcome is dependent upon the studies selected for review, and on how the studies as well as the reviewers define the people, interventions, and outcomes of interest. Interpretation of results is dependent upon the validity of the included studies and other characteristics and as most Cochrane Reviews focus on randomised trial data it is necessary to concentrate on the appraisal of the validity of such data.

In the context of a systematic review, the validity of a study is the extent to which its design and conduct are likely to prevent systematic errors, or bias. An important issue that should not be confused with validity is precision. Precision is a measure of the likelihood of random errors. It is reflected in the confidence interval around the estimate of effect from each study and the weight given to the results of each study when an overall estimate of effect or weighted average is derived using meta-analysis. More precise results are given more weight. Variation in validity can explain variation in the results of the studies included in a systematic review. More rigorous studies may be more likely to yield results that are closer to the "truth". Quantitative analysis of results from trials of variable validity can result in "false positive" conclusions (erroneously concluding an intervention is effective) if the less rigorous studies are biased toward overestimating an intervention's effective-

ness. They might also come to "false negative" conclusions (erroneously concluding no effect) if the less rigorous studies provide less precise or biased estimates of an intervention's effect. It is important to systematically complete critical appraisal of all studies in a review even if there is no variability in either validity or results of the included studies

There are four sources of systematic errors in trials of the effects of healthcare:

1. In order to prevent selection bias an appropriate method for preventing foreknowledge of treatment assignment is crucially important in trial design. The ideal is for the process to be impervious to any influence by the individuals making the allocation. Thus, trials can be judged on the reported method of allocation concealment. When reviewers enter studies into Review Manager (RevMan) they are required to enter whether allocation concealment was adequate (A), unclear (B), inadequate (C), or that allocation concealment was not used (D) as a criterion to assess validity.
2. Performance bias refers to systematic differences in care provided to comparison groups other than the intervention of interest. To protect against unintended differences in care and placebo effects, those providing and receiving care can be "blinded" so that they do not know the group to which the recipients of care have been allocated. Blinding is likely to be particularly important in research with subjective outcome measures such as pain.
3. Attrition bias refers to systematic differences between groups in losses of participants from the study. Because of inadequacies in reporting how losses of participants are handled, reviewers should be cautious about implicit accounts of follow-up. The approach to handling losses has great potential for biasing the results and reporting inadequacies cloud this problem. Thus reviewers should be cautious about using reported follow-up as a validity criterion.

4. Detection bias refers to systematic differences in outcome assessment. Trials that blind outcome assessors regarding treatment allocation should logically be less likely to be biased than trials that do not. Somewhat different from bias in outcome assessment is bias due to selective reporting of results. Therefore, reviewers may want to consider specification of predefined primary outcomes and analyses by the investigators indicators of validity

There are several ways to rate validity of studies. One is to rate individual criteria as "met", "unmet", or "unclear" and to use individual criteria, such as adequacy of allocation concealment, in sensitivity analyses. In general and when possible, reviewers should obtain further information from the authors of a report when it is unclear whether a criterion was met. There is no "gold standard" for the "true" validity of a trial; the possibility of validating any proposed scoring system for quality is limited. None of the currently available scales for measuring the validity or "quality" of trials can be recommended without reservation. Most of the available scales for assessing the validity of randomised controlled trials derive a summary score by adding the scores (with or without weights) for each item. While this approach offers appealing simplicity, it is not supported by empirical evidence.

The logical reason for focusing on randomised controlled trials in Cochrane Reviews is that randomisation is the only means of allocation that controls for unknown and unmeasured confounders as well as those that are known and measured. Albeit differences between comparison groups in prognosis, responsiveness to treatment or exposure to other factors that affect outcomes can distort the apparent magnitude of effects of the intervention of interest.

Several basic decisions must be made regarding the critical appraisal studies; similar to those made regarding the process of selecting studies. As a general rule, the Collaboration recommend that at least two reviewers assess information that involves subjective interpretation and information that is critical to the interpretation of results (e.g., out-

come data). It is important to test any assessment criteria that are planned on a pilot sample of articles to ensure that the appraisal criteria can be applied consistently. Although experts in content areas may have pre-formed opinions that can bias their assessments but they may nonetheless give more consistent assessments of the validity of trials than persons without content expertise and they may have valuable insights that are different than those that someone with methodological expertise alone would have. It may seem desirable to use both content experts and non-experts and to ensure that both have an adequate understanding of the relevant methodological issues. Reviewers must also decide whether those assessing study validity will be blinded to the names of the authors, institutions, journal and results of a trial when they apply critical appraisal criteria to the methods.

There are several ways in which validity assessments can be used in a review: as a threshold for inclusion of studies; as a possible explanation for differences in results between trials; in sensitivity analyses; as weights in statistical analysis (meta-analysis) of the results. Failure to meet one or more validity criteria may indicate such a high risk of bias in some reviews that it constitutes grounds for exclusion of those studies and if reviewers raise the methodological cut-point for including studies, there will be less variation in validity among the included reports. There are two major difficulties with critically appraising the validity of studies. The first is inadequate reporting of trials and reviewers should attempt to obtain additional clarifying data from investigators. The second limitation, which in part is a consequence of the first, is limited empirical evidence of a relationship between parameters thought to measure validity and actual trial outcomes. Reviewers should therefore avoid the use of "quality scores" and undue reliance on detailed quality assessments (Mulrow and Oxman 1997f)

4.4.3.1 Commentary: The critical appraisal of studies was carried out according to the Cochrane Handbook guidelines current at the time of conducting this review, and were similar to those shown above,

if in a different format, and are described in full in the review. The following parameters were appraised being those relating to applicability of findings, validity of individual studies and design characteristics that could affect the interpretation of results. The appraised parameters were recorded on the data collection forms (Appendix B (ii)) together with data collection information as discussed below.

Whether a review's findings are applicable to a particular population, intervention or outcome depends upon the studies selected for the review and the validity of data extracted. The validity of each study was assessed by the extent to which its design and conduct were likely to prevent the four most common systematic errors or bias:

- a. the trials were judged on the reported method of allocation concealment (selection bias) as adequate (A), unclear (B), inadequate (C) or not used (D) ready for entry into RevMan software
- b. the trials were judged on the protection given to prevent unintended differences in care and placebo effects (performance bias) by those providing and receiving care by adequate 'blinding'. This was particularly important in this review when assessing a subjective outcome measure such as pain.
- c. the approach to handling losses and dropouts from studies (attrition bias) was assessed because of the potential for biasing the results
- d. and finally did adequate blinding of outcome assessor's control systematic differences in outcome assessment (detection bias)? Was selective reporting of results evident?

The initial validity of studies was rated by assessing each criteria as 'met', 'unmet' or 'unclear' and further information was requested and obtained from four of the six authors of the included studies. At the protocol stage we had decided not to use a scoring system for quality because of its limitation insofar as they were not supported by empirical evidence. This was agreed by the editorial review team at the time of protocol submission and acceptance but a quality review was

requested post hoc and this was reluctantly carried out in order to secure acceptance of the review and entry into the Cochrane Library. This and other issues surrounding the editorial review are discussed in more detail in section 4.6. On this basis, the six randomized controlled trials meeting the inclusion criteria for this systematic review and meta analysis were rated for experimental design quality using the Reeve et al. (1995) scale (see Appendix B iii), a modification of a scale originally published by Chalmers et al (1981). Reeve's (1995) modified scale was first used in a Technology Assessment of Transcutaneous Electrical Nerve Stimulation by the Canadian Co-ordinating Office for Health Technology Assessment.

As described earlier three content area reviewers carried out the initial critical appraisal, after the pilot study, and selection of studies for the review. However one of the reviewers was unable to continue with the final analysis and preparation of the review due to a conflict of interest arising (business) which was not however, related to the conduct of this Cochrane Review. Two reviewers (JGG and MWF) completed the review and it became self-evident that content area reviewers were essential in order to understand and evaluate the application of TENS/ALTENS and the electrical parameters involved. This was a situation that did not appear to be fully understood by members of the Cochrane Back Subgroup of the CMSG editorial team when their comments were considered and evaluated in some detail and these issues are discussed again later (4.6).

Reviewers assessing study validity were not blinded to the names of authors, institutions, journals or results of trials as discussed in the previous section. The reviewers consider this decision to be the correct one, in view of the multiple publications of several of the studies (one article was re-published fifteen years after the trial had ended!) to be reviewed. These validity assessments were used as a threshold for inclusion of studies in the review, as a possible explanation for differences in results between trials, in sensitivity analyses

and as weights in statistical analysis (meta-analysis) to be discussed in the following sub-sections.

The two major difficulties appraising the validity of studies were:

- a. inadequate reporting of trials was overcome by seeking additional clarifying data from the principal investigators and
- b. the limited empirical evidence of a relationship between parameters thought to measure validity and actual trial outcomes was overcome initially by avoiding the use of a quality scoring system and placing undue reliance on a quality assessment.

A post hoc study quality scoring system was instigated on the instructions of the editorial review but this does not appear to contribute to the validity of the final version of this Cochrane Review.

4.4.4 Collecting data

The data collection form is a bridge between what primary investigators have reported and what a reviewer ultimately reports. This form is directly linked to and is therefore a visual representation of the formulated review question and planned critical appraisal of included studies, it is the historical record of the multitude of decisions that occur throughout the review process and finally it is the data repository from which the analysis will emerge. Given the important functions of data collection forms, ample time and thought should be invested in their design.

Both electronic and paper forms can be designed to provide an historical record of decisions and refinements that occur throughout the review process. Many reviewers use a double-abstraction process whereby two independent appraisals of each study can be compared and reconciled if necessary.

A variety of software and data management programs may be helpful in the systematic review process, such as Reference Manager and ProCite but the software that is essential for every Cochrane Re-

view is RevMan. This software facilitates data management, quantitative analyses, and report generation. RevMan is provided at no cost to reviewers in Collaborative Review Groups and Cochrane Centres offer RevMan workshops.

When adapting or designing a data collection form reviewers first should consider how much information they want to collect. Overly detailed collection can result in forms that are longer than original study reports, tedious, boring, and wasteful of reviewer time. On the other hand, if forms are not sufficiently detailed and omit key data, reviewers may have to re-abstract studies using supplemental data collection forms. Every Cochrane Review is assigned a unique identifier, which must be entered into RevMan when entering information about references, included and excluded studies tables, data tables etc. The same identifier should be used for all reports referring to the same study. Reviewers may need to collect data from multiple reports of the same trial and to keep a record of the key source information. Unpublished information that is used should be written and should be coded in the same way as published information.

Although the search and selection process should have weeded out most ineligible studies, it is good practice to verify study eligibility at the time of data abstraction or collection. Verification information should occur early because the remainder of the form pertains to studies that meet inclusion criteria. Cochrane Reviews include an excluded studies table and the verification information on the data collection form can be a mechanism for coding reasons why such studies were excluded. For example, a reviewer may only include truly randomised trials in a review. A verification query on the data collection form might be: Randomised? Yes, No, Unclear.

When critically appraising each study, it is necessary to code specific study characteristics. These characteristics can be categorized into groups that match information that will be entered into RevMan: methods, participants, interventions, and outcomes. Information under participants often includes data relevant to the study setting and diag-

nostic criteria for the condition of interest. Data that is collected should be directly linked to the review question(s) and planned analysis strategies.

Different research methods can influence study outcomes by introducing bias and artefacts in study results. For example, whether allocation was adequately concealed is important. When entering information about particular studies in RevMan, it will be necessary to code allocation concealment as adequate (A), unclear (B), inadequate (C) or not used (D). Data collection forms should reflect these assessments. Other methods features that may be relevant to collect include study duration; type of trial such as parallel or cross-over design; patient, provider and outcome assessor blinding; amount of drop-outs and cross-overs; cointerventions and other potential confounders. The methods part of the data collection form should include the validity criteria that are used.

Characteristics of participants may vary substantially across studies; items that should be collected are those that could affect study results or help users assess applicability. Typical items that are useful for assessing applicability include age and gender. If the settings of studies are likely to influence treatment effects or applicability, they should be assessed. Diagnostic criteria that were used to define the condition of interest can be a particularly important source of clinical heterogeneity and should be described.

The intervention and how it was delivered should be described. Treatment length also may be recorded here, particularly if it was different than study follow-up length and was not recorded under methods. For trials that do not utilise placebos and those that evaluate complicated interventions, it is also important to collect information regarding what was given to the control group. This will help guide later decisions about whether it is reasonable to combine data across studies; marked heterogeneity in what is received by control groups may be a reason for not combining studies, or for doing sensitivity analyses.

Researchers of primary studies often report more than one out-

come (mortality, morbidity, quality of life, etc.), may report the same outcome using different measures, may include outcomes for sub-groups and may report outcomes measured at different points in time. The reviewer needs to integrate what type of outcome information is needed to answer the review's question(s) with what can be anticipated in the reports of studies. For cross-over trials and trials with outcome assessments at various periods of follow-up, decisions will need to be made about which outcomes to assess.

Accurate coding is extremely important. Reviewers need instructions and decision rules on the data collection form. It is crucial for reviewers to practice using the form and receive training if a different reviewer designed the form.

All forms should be pilot tested using a representative sample of the studies to be reviewed. When multiple reviewers are participating on a project, there may need to be a consensus among reviewers before the form is modified to avoid any misunderstandings or later disagreements. In fact, it is rare for a data collection form to not require any modifications after it has been piloted but it may only be necessary to clarify coding instructions without modifying the actual data collection form.

Reliability refers here to the degree to which different persons review a study in the same way. When more than one person is reviewing data, there will inevitably be disagreements and multiple reviewers need to develop a plan for comparing information in their data collection forms and for reaching consensus when there are disagreements (Mulrow and Oxman 1997g)

4.4.4.1 Commentary: A paper data collection form was used for this review and is shown in full in Appendix B (ii). A triple extraction process was used whereby three independent appraisals of each study was made for comparison and reconciliation of any differences, by a majority decision of 2:1, and the data was entered into the Cochrane Collaboration Review Manager (RevMan) software to facilitate data

management, quantitative analyses and report generation.

The data collection form went through the usual design and adaptation procedures to produce a suitable collection tool for the trials contributing to this review. Initially we had three pages:

1. A reviewers check list sheet which identified the reviewer, the key characteristics of the types of participants, the key characteristics of the types of intervention, the key characteristics of the types of outcome measures and the methodological quality of the study for weighting the meta-analysis.
2. The second sheet, which was later abandoned as we became more adept at data extraction, was used as a checklist for completing sheet 3, which described the information required from the trials contributing data to the review.
3. The third sheet was used to record the data collected from the trials contributing to the review, included and excluded trials, and included the following information: details of the trial, methodology, participants, comparison groups, outcomes and notes ready for input into the RevMan software.

The data collection forms, following minor adjustments after the pilot study, were found to be quite adequate for the collection of key data for this review. There was no necessity to use supplemental data abstraction forms, until we were advised post hoc, that a quality review was required to meet the requirements of the Cochrane editorial team, for inclusion of the Review in the Cochrane Library. This request was described in the previous section and a supplemental data extraction form for rating the quality design of the six included studies in the review was constructed (Appendix B (iii)). Unpublished information was requested from the six authors of the included studies and this data was written up and coded in the same way as published information.

Verification of study eligibility, on the basis of being truly randomised controlled trials, was confirmed, and recorded on the data

collection sheets at the time of data extraction. Data from the non-randomised studies was also recorded in preparation for entry into the RevMan software to prepare an excluded studies table. Trial details of author, dates, published or unpublished information or a mixture of both was also recorded at this time.

Some specific study characteristics e.g. of methods, participants, interventions and outcomes, were coded as necessary e.g. allocation concealment being coded as adequate (A), unclear (B), inadequate (C) or not used (D) and recorded on the data collection form.

Other appropriate methodological features were also collected including study duration, type of trial such as parallel or cross-over design, patient, provider and outcome assessor blinding, number and management of dropouts and cross-overs, cointerventions and other potential confounders, adequacy of sample size, assessment methods and intention to treat analyses. The methods part of the data collection form thus included the validity criteria, that was used for each study assessed, by the extent to which its design and conduct were likely to prevent the four most common systematic errors or bias discussed in the previous section.

The characteristics of participants included age and gender, numbers in trial, setting, country, diagnostic criteria, duration of chronic low back pain, adequacy and comparability of source population, adequacy of baseline matching and meeting inclusion/exclusion criteria.

The intervention and how it was delivered e.g. as TENS or ALTENS or a mixture of both - as defined in the protocol, i.e. high frequency, low-intensity TENS or low-frequency high-intensity ALTENS, description of other electrical parameters, treatment length and number of treatments given, standardisation of the intervention, information on control groups, appropriateness of control group and the credibility of the placebo intervention were assessed.

The outcome measures were assessed for appropriateness and validity to answer the reviews' questions in relation to pain control

and function and follow up assessments as numbers of patients improved and not improved in comparison with the placebo controlled groups, together with numbers returning to work and side effects.

There were remarkably few differences in the quality and reliability of data extraction between the three reviewers, perhaps this was a reflection on using content area specialists as reviewers, and any minor differences were resolved by a majority decision as discussed earlier.

In addition, the six randomised controlled trials meeting the inclusion criteria for this systematic review were rated by a post hoc quality assessment as requested and described in the previous section of the thesis.

The resulting data was inputted to the RevMan software in accordance with the RevMan manual and the systematic review and meta-analyses were made on this database of studies. These studies, included and excluded are described in detail in the following accompanying Cochrane Review (4.5) in the sub-sections headed description of studies, methodological qualities of studies and characteristics of included and excluded studies. The RevMan software then analysed the six trials included in this review and this is described below.

4.4.5 Analysing and Presenting Results

The reason for conducting reviews systematically is to ensure that the results are valid. The role of statistical analysis in reviews may be less clear and sometimes reviewers and users of reviews in their rush to get to the summary statistic lose sight of the importance of reflection and judgement in the steps preceding analysis, in the analysis itself, and in drawing conclusions. To prepare a review investigators must collect data from individual studies, just as they must collect data from individual patients in primary studies. In either case, statistical methods can be used to analyse and summarise data. If used appropriately, they provide a powerful tool for deriving meaningful conclu-

sions from the data and help prevent errors in interpretation. A common error when statistical methods are not used in reviews is to compare the number of "positive" studies with the number of "negative" studies. With such a "vote counting" approach, a study may be counted as "positive" in one review and "negative" in another, depending on how the results are interpreted by the reviewers. There is also a tendency to overlook small but clinically important effects when counting votes, particularly when counting studies with statistically "non-significant" results as "negative". Another error that can easily occur when statistical methods are not used is inappropriate weighting of the results of the individual studies. It is also possible for a reviewer to introduce bias by inappropriately stressing the results of one study over another when using non-quantitative methods.

A systematic review that does not include a statistical analysis can be just as valuable as a meta-analysis for this is only one element of a summary. The most important reasons for not using meta-analysis in a review are the lack of relevant, valid data. In general, if it is not clear how the results of a meta-analysis will help people making decisions, it should not be done. While the use of statistical methods in reviews can be extremely helpful, the most essential element of an analysis is a thoughtful approach, to both its qualitative and quantitative elements.

The first and most important step in planning the analysis is to specify the comparisons that will be made. These should relate clearly and directly to the questions or hypotheses that are posed when the objective of the review is formulated. Decisions about which study results are similar enough that they should be grouped together require an understanding of the problem that the review addresses and judgement. Essentially the same considerations apply to deciding what comparisons to make, what outcomes to combine and what key characteristics (of participants, interventions, outcomes and study design) to consider when investigating heterogeneity (variation in effects). These considerations must be addressed when setting up a Table of Comparisons

using the Review Manager software (RevMan) and in deciding what information to put in the Table of Included Studies.

Having specified the comparisons that will be made, the next step in the analysis is to prepare tabular summaries of the data. Because concealment of allocation is a validity criterion that applies to all outcomes, and there is good evidence to support the logical arguments for using this criterion, it is assigned by reviewers when study references are entered in RevMan and automatically assigned to studies in tables of results as one characteristic by which studies can be sorted.

In general, reviewers should first determine which way of reporting results is most likely to be intuitively understandable and useful to people making decisions. So far as possible, results should be transformed or data should be sought from investigators so that all of the study results can then be presented in that way.

Having decided what comparisons to make and what data are needed for each comparison, the next question to ask is whether the results of studies are similar within each comparison. Are the differences among the results of the studies greater than could be expected by chance? One way of doing this is to look at a graphical display of the results. If the confidence intervals for the results of each study (typically presented by horizontal lines) do not overlap, it suggests that the differences are likely to be "statistically significant". RevMan will automatically test the homogeneity of the results of the individual studies being combined for each comparison of dichotomous or continuous data. Irrespective of the extent of heterogeneity in results, it is frequently of interest to examine a particular category of participants in a review. These examinations, or subgroup analyses, are exceedingly common, but they are also often misleading. Conclusions based on subgroup analyses can do harm both when a particular category of people is denied effective treatment (a "false-negative" conclusion), and when ineffective or even harmful treatment is given to a subgroup of people (a "false-positive" conclusion). Because of these risks and the frequency of their occurrence, reviewers need to be cautious about doing subgroup analyses

and about interpreting the results of the ones that they feel compelled to do. Reviewers should, so far as possible, attempt to state any hypotheses they have about potentially important differences in subgroup response *a priori* (in the protocol for the review).

Differences in subgroup response observed within a single study provide a stronger basis for drawing conclusions, and if a difference is observed across a number of high quality studies it strengthens a conclusion that the difference is real.

The central aim of most Cochrane Reviews is to provide a reliable estimate of the effects of an intervention or type of intervention, based on a weighted average of the results of all the available good quality studies. If it makes sense to combine the results of a group of studies and the observed differences between the results of the studies are not statistically significant or practically important, it is relatively straightforward to combine the results. Each study is summarised using a measure of effect (such as an odds ratio, a relative risk or a mean difference) that represents the within study comparison of the intervention and control groups. In this way participants in each study are only compared to people in the same study.

The confidence interval around an estimate derived from an appropriate statistical synthesis indicates how precise that estimate is. One important consideration that arises in meta-analyses is whether to incorporate between study variation in estimating the confidence interval (a "random effects" approach). If there is little between study variation (i.e. the test for homogeneity results in a large *p* value, say greater than 0.10), this will make little difference. If there is significant between study variation, an analysis that ignores this (a "fixed effects" approach) will give a narrower confidence interval than one that does not. If there is significant heterogeneity reviewers should be cautious about interpreting the overall estimate derived from a meta-analysis, as well as attributing between-study differences to any one factor. There is disagreement on how to summarise the results of studies, and whether they should be combined when there is substantial heterogeneity. Re-

viewers should alert readers of their review when there is substantial heterogeneity, and they should encourage cautious interpretation of the aggregated results. Reviewers should attempt to explore the reasons for the heterogeneity and to explain it, but the interpretations must be cautious because the analyses are usually *post hoc*. One potential explanation for heterogeneity that can be investigated in an *a priori* fashion is methodological quality. Differing methodological quality in the component studies could produce both bias and accompanying heterogeneity. If there are important differences in the quality of studies, reviewers should consider excluding poorer quality studies. It is generally agreed that the fixed effects approach for a test of significance for the overall null hypothesis ("no effect in all studies") is statistically valid. A statistically significant result indicates that a treatment effect exists in at least one of the studies. Whether heterogeneity is present or not, the overall typical effect measure from a fixed effects approach is an informative average measure of treatment effect. The random effects methods rely on assumptions that the studies are a random sample from a hypothetical population of studies and that the heterogeneity between studies can be represented by a single variance. Moreover, a pragmatic concern is that the "random effects" methods give more weight to the smaller studies than the "fixed effects" methods and smaller studies are often of poorer quality and may be more susceptible to publication bias. That leaves as the primary dispute the different approaches to the calculation of a confidence interval around a typical effect measure when there is clear heterogeneity. If the test of heterogeneity is statistically significant and the differences in results are practically important:

1. Reviewers should consider the sources of the heterogeneity (e.g. differences in dose, timing of treatment, length of treatment, participant characteristics). In particular, reviewers should explore whether differences in the control of bias among the studies explain the heterogeneity (e.g. concealment of randomisation).
2. If the heterogeneity can be explained, reviewers should consider (with due caution) the option of presenting the results of subgroup

analyses.

If the heterogeneity cannot be explained, reviewers should consider the following options:

1. Do not aggregate the studies at all.
2. Use the fixed effects model with appropriate cautious interpretation.
3. Use the random effects model with appropriate cautious interpretation.
4. Use both the fixed and random effects models as an additional aid in explaining the uncertainty around an analysis with heterogeneous studies.
5. Whatever is done, reviewers should clearly explain what was done and why (Mulrow and Oxman 1997h)

4.4.5.1 Statistical methods available in Review Manager/CDSR

Meta-analyses use a variety of techniques. Unfortunately, there is not one "correct" technique. The choice of technique depends on the nature of the data being analysed. Fortunately, as with other uses of statistics, a conceptual understanding of the principles is more important than detailed knowledge of the specific techniques. The statistical methods available in RevMan 3.0 include:

Type data	Summary statistic	Model	Method
Dichotomous	odds ratio (O-E)	fixed effect	Peto
			Mantel-Haenszel
		random effects	DerSimonian and Laird
	relative risk	fixed effect	Mantel-Haenszel
		random effects	DerSimonian and Laird
	risk difference	fixed effect	Mantel-Haenszel
		random effects	DerSimonian and Laird

Continuous	Weighted mean difference	fixed effect random effects	inverse variance DerSimonian and Laird
	Standardised mean difference	fixed effect random effect	inverse variance DerSimonian and Laird
Individual patient data	odds ratio (O-E)	fixed effect	Peto

Figure XVII: Table of statistical methods available in RevMan

For dichotomous data there are pros and cons for each of the summary statistics: odds ratio, relative risk, risk difference. Although the odds ratio has been commonly used in meta-analysis, there are concerns about the potential for invalid clinical interpretation of the odds ratio. The odds ratio has statistical advantages relating to its sampling distribution and its suitability for modelling, but these advantages are not always important in meta-analyses. Moreover, there is no solid basis for assuming that the odds ratio is more constant across studies than other summary statistics. In summary, while it may be desirable to maintain consistency across reviews with regard to the use of statistical methods and presentation of results, it is difficult to justify restricting analyses to any particular method.

For some reviews it may be useful to undertake an analysis that is not supported by RevMan. When such an analysis is done it should be described and referenced in the methods section of the review and the results should be reported in the text of the review.

Because there are different approaches to conducting a systematic review, reviewers should ask: "How sensitive are the results of the analysis to changes in the way it was done?" This provides reviewers with an approach to testing how robust the results of the review are relative to key decisions and assumptions that were made in the process of conducting the review. Each reviewer must identify the key decisions and assumptions that are open to question, and might conceiva-

bly have affected the results, for a particular review:

1. changing the inclusion criteria (including the types of participants, interventions and outcome measures, and methodological cut-points)
2. including or excluding studies where there is some ambiguity as to whether they meet the inclusion criteria
3. excluding unpublished studies
4. excluding studies of lower methodological quality
5. reanalysing the data using a reasonable range of results for studies where there may be some uncertainty about the results (e.g. because of inconsistencies in how the results are reported that cannot be resolved by contacting the investigators or because of differences in how outcomes are defined or measured)
6. reanalysing the data imputing a reasonable range of values for missing data
7. reanalysing the data using different statistical approaches (e.g. using a random effects model)

Although several ways of examining the potential impact of publication bias on the results of a systematic review have been described, all of them are problematic. Nonetheless, reviewers may want to consider using a "funnel plot" to look for publication bias if there is a sufficient number of studies. This can be done by plotting the study weight (one divided by the variance of the odds ratio) or sample size (on the "y" axis) against the odds ratios (on the "x" axis). Typically this will give the appearance of a funnel with larger studies (with greater weights) at the top in the middle and smaller studies spread out at the bottom. A gap at the bottom of the funnel on the right side (assuming smaller odds ratios (less than one) represent beneficial effects) indicates that small "positive" studies were identified, whereas equal numbers of small studies in the opposite direction were not.

If the sensitivity analyses (see Appendix B (iv)) that are done do not materially change the results, it strengthens the confidence that can be placed in them. If the results change in a way that might lead to different conclusions, this indicates a need for greater caution in inter-

preting the results and drawing conclusions. It might also enable reviewers to clarify the source of existing controversies about the effectiveness of an intervention, or lead reviewers to hypothesise potentially important factors that might be related to the effectiveness of the intervention and warrant further investigation.

Three types of data may be missing in a review: unidentified studies, information for estimating the magnitude of effects, and information about characteristics that may be related to the magnitude of effects. Methods for handling missing information in the studies that are identified include excluding studies for which data are missing, simple imputations and complex strategies for imputing values for the missing data.

Cross-over trials can present a problem, particularly if both cross-over and parallel group trials are included together. One approach to this problem is to treat the cross-over studies in the same fashion as parallel group studies. That is, results from the treatment period can be handled as if they came from one group of patients and results from the control period can be treated as if they came from an independent group of patients. However, this approach ignores the fact that it is the same patients in both arms of the study and they are not independent of each other.

The analytic methods that are used in reviews should be described in the Methods section. The main results should be described and clarified in the text. Reviewers should be careful to ensure that the focus in the Results section is consistent with the reviews' objectives and the comparisons specified in the protocol of the review. Post hoc analyses should be reported as such. Cochrane Reviews contain the actual data entered into the Data Tables by reviewers. Tables and graphs that are displayed in RevMan and CDSR are generated "on the fly" using MetaView software.

There is a convention in CDSR of displaying summary statistics for unfavourable outcomes so that for dichotomous data odds ratios and relative risks less than one (and risk differences less than zero) indicate that treatment is better. In graphical displays this is represented by es-

timates indicating that treatment is better than control on the left side of the vertical line indicating no difference. Both reviewers and users of the reviews can be confused when this convention is not maintained and there is a greater risk of errors being made. However, there are circumstances where it may not be appropriate to adhere to this convention and it sometimes makes more sense to present the results for "good" outcomes (Mulrow and Oxman 1997h)

4.4.5.2 Commentary: The analyses and presentation of results of this systematic review are described in full in the Cochrane Library Review format which follows this section. This sub-section considers the importance of reflection and judgement in the steps preceding analysis, in the analysis itself and in drawing the conclusions. The statistical meta-analysis is only one element of a systematic review summary, albeit an important element in those reviews which are suitable for this, but it is most important to consider the thoughtful approach to both its qualitative and quantitative elements too. In this review of 68 studies only six were suitable for meta-analysis, a very small number considering the database we had to work with, nonetheless the evaluation of the other 62 less powerful uncontrolled studies also contribute to the final analysis.

The ten comparisons specified to relate directly to the research questions are listed in the review albeit it was only possible to make five comparisons in the final analysis due to lack of suitable data and are shown below using a fixed effects (Peto) model (see also page 564):

1. The use of TENS treatment for chronic low back pain is more effective than placebo for reducing pain with an OR 1.62 (0.90, 2.68).
2. The use of ALTENS treatment for chronic low back pain is more effective than placebo for reducing pain with an OR 7.22 (2.60, 20.01).
3. The use of TENS/ALTENS treatment for chronic low back pain is more effective than placebo for reducing pain with an OR 2.11(1.32, 3.38).

4. Insufficient data to evaluate the efficacy of TENS for improving the range of movement in this group of patients.
5. The use of TENS treatment for improving the range of movement for these patients pain gave an OR 6.61(2.36, 18.55).
6. Insufficient data to evaluate the efficacy of TENS/ALTENS for improving the range of movement in this group of patients.
7. Insufficient data to evaluate the efficacy of TENS for improving functional status, well being and return to work in this group of patients.
8. Insufficient data to evaluate the efficacy of ALTENS for improving functional status, well being and return to work in this group of patients.
9. Insufficient data to evaluate the efficacy of TENS/ALTENS for improving functional status, well being and return to work in this group of patients.
10. The use of TENS/ALTENS for chronic low back pain is relatively free from side effects in comparison to a placebo.

Decisions about which studies were similar enough to be grouped together were made by the content area specialist reviewers who were thus enabled to understand the problems of the review, what comparisons to make, what key characteristics (of participants, interventions, outcomes and study design) to consider when investigating heterogeneity, and to make appropriate judgements based on their clinical and academic expertise. These considerations were addressed before setting up the Table of Comparisons in the RevMan software. Concealment of allocation being a validity criterion that applies to all outcomes was automatically assigned to all studies entered into RevMan. The cross-over trial (Thorsteinsson 1977) was treated in the same way as a parallel group study i.e. results from the TENS treatment period were treated as if they came from one group of patients and results from the control period treated as if they came from an independent group of patients.

The graphical displays for each comparison were examined at this stage and this showed the confidence intervals overlapping which suggests that the differences among the results would unlikely to be 'statistically significant' with RevMan automatically testing the homogeneity of the results of the individual studies being combined for each comparison of dichotomous data. Subgroup analyses were restricted to TENS and ALTENS and these were stated *a priori* in the protocol.

The central aim of this Cochrane Review was to provide a reliable estimate of the effects of TENS and ALTENS for the treatment of chronic low back pain, based on a weighted average of the results of the six good quality studies identified during the review process. Each study was summarised in RevMan using a measure of effect, i.e. the odds ratio, which represented the within study comparisons of the TENS/ALTENS intervention and control groups, together with their 95% confidence intervals using a fixed-effect (Peto) approach. It is, however, necessary to interpret the aggregated results of these six studies with some caution because of the small number of participants involved, the heterogeneity of non-specific diagnoses and the quality of the studies combined. However, these results do represent the best available evidence we have at this moment in time as discussed in the final section of this thesis.

In respect of sensitivity testing, i.e. 'how sensitive are the results of the analysis to changes in the way it was done', the following key decisions were examined and assessed to identify their effects on this review:

1. Would changing the inclusion criteria e.g. types of participants, interventions and outcomes affect this review. The diagnosis of low back pain is an ill-defined one and many of the subjects in this review were also failed back pain surgery patients, interventions were not standardised across studies and outcome measures varied between studies. Exclusion of failed back surgery subjects; non-standardised interventions and specific outcomes would have reduced the number of studies and subjects

to a level where review and meta-analysis would have been less likely.

2. Would including or excluding studies, where there was some ambiguity, affect this review. The reviewers closely followed the criteria as laid down in the protocol and deviating from this would almost certainly have weakened the precision of this review but see Appendix B (iv) - sensitivity testing.
3. No unpublished studies were identified after contacting several specialists in this field both in the UK and other countries.
4. No non-English language studies were identified in the searched databases specified in the review or from citation tracking of the initial 68 identified studies. It would appear that searches of non-English language databases would be the only solution for identifying further studies but this was beyond the resources of the review team and possibly even the resources of the Cochrane Collaboration at that time.
5. Would the exclusion of lower methodological quality studies have affected the review? All studies included in this review must have met the exacting inclusion/exclusion criteria specified in the protocol and the inclusion of lower methodological studies would have weakened the quality of the review. However in order to strengthen the confidence that can be placed in these results a sensitivity analysis was conducted on comparison 1 and 3 (Figure XVI also see Appendix B (iv)) by excluding the two studies of lowest methodological quality included in this review and the results of this are as follows:

Comparison 1 (TENS v Placebo)=	all studies	Peto OR
1.52(0.90, 2.58)		
Comparison 1 (TENS v Placebo)=	- Jeans 1979	Peto OR
1.53(0.89, 2.62)		
Comparison 1 (TENS v Placebo)=	- Jeans 1979	Peto OR
1.39(0.79, 2.46)	- Marchand 1993	

Comparison 3 (ALL* v Placebo) =	- all studies	Peto
OR 2.11(1.32, 3.38)		
Comparison 3 (ALL* v Placebo)=	- Jeans 1979	Peto OR
2.14(1.33, 3.45)		
Comparison 3 (ALL* v Placebo)=	- Jeans 1979	Peto OR
1.94(1.18, 3.17)	- Marchand 1993	
*ALL = TENS and ALTENS Combined		

Figure XVIII: Table of sensitivity testing by exclusion

Would re-analysing the data using different statistical approaches have affected the results and the conclusion drawn. To answer this question the data was reanalysed in RevMan using a random effects model, which takes both within and between study variations into account in determining the level of uncertainty (see page 572) and the results of this are as follows:

Comparison 1 (TENS v Placebo)	Fixed	Peto OR
1.52(0.90, 2.58)		
Comparison 1 (TENS v Placebo)	Random	OR
1.52(0.89, 2.61)		
Comparison 3 (ALL v Placebo)	Fixed	Peto OR
2.11(1.32, 3.38)		
Comparison 3 (ALL v Placebo)	Random	OR
2.68(1.23, 5.82)		
Comparison 3 (ALL v Placebo)	Bayesian	OR
3.86(1.46, 13.74)		

Figure XIX: Table of sensitivity testing using random effects model

6. A Bayesian analysis, which bears some similarities to a random effects model, (see page 555) was also undertaken on the six studies included in this review (plus one small study (Lerner 1981) which was subsequently excluded from the final review)

by Philip Jarvis of the De Montfort Universities Department of Medical Statistics using the BUGS/CODA software (Jarvis et al 1996). To collate the information from the seven placebo controlled studies, a crude efficacy measure was chosen based on the number of subjects showing improvement i.e. a significant reduction in the levels of low back pain. They concluded that the posterior estimate for the population increase in odds of improvement on ALTENS/TENS compared to placebo was 3.86 (mid-95% credible interval 1.46 to 13.74). This result suggested a potential benefit for the use of ALTENS/TENS in the treatment of chronic low back pain.

A result not dissimilar, if somewhat more positive, than the systemic review and meta-analysis under consideration in this thesis. If we add the excluded study (Lerner 1981) to the six studies in RevMan and calculate again we have the following estimations, which again are not dissimilar, with the Random effects model the nearest to the Bayesian method:

Comparison 3 (ALL v Placebo)	Bayesian	OR
3.86(1.46, 13.74)		
Comparison 3 (ALL v Placebo)	Fixed	Peto OR
2.66(1.72, 4.13)		
Comparison 3 (ALL v Placebo)	Random	OR
3.97(1.57, 10.05)		

However, the credible interval for the Bayesian (and for the similar Random Effects model) estimate is extremely wide and reflects both the small number of studies and small sample sizes. This study ends with the recommendation to run a large randomised placebo controlled study assessing the effectiveness of ALTENS/TENS in the treatment of chronic low back pain.

7. The sensitivity analyses described above did not materially change the results of this meta-analysis and in fact strengthens

the confidence that can be placed in the results. If the results had changed in a way that might lead to different conclusions then this would have indicated a need for greater caution in our interpretation of the results and the resulting conclusions. It might also have enabled the reviewers to clarify the source of existing controversies about the effectiveness of these interventions or lead us to hypothesise potentially important factors that might be related to the effectiveness of these interventions that warrant further investigation.

Although the highest rated study for quality in this review (Deyo/Walsh 1990) may be seen as a 'negative' study and had not suffered from publication bias, there were insufficient numbers of other randomised controlled studies, meeting the inclusion criteria, to consider using a 'funnel graph' to test the potential impact of publication bias on the results of this systematic review. The analytic methods used in this Review are described in the Methods section, tables and graphs were generated using MetaView software, printed from the Cochrane Library on CD-ROM and are included at the end of the following review (4.5). Lastly, whilst there is a convention in the CDSR to display summary statistics for unfavourable outcomes it seemed more appropriate not to adhere to this convention for this review and to display 'good' outcomes instead. The main results are also interpreted in the next sub-section.

4.4.6 Interpreting results

Although it can be argued that the results of a systematic review should stand on their own, many people faced with a decision look to the discussion and conclusions of a review for help interpreting the results. Because Cochrane Reviews have an international audience, the discussion and conclusions should, so far as possible, assume a broad international perspective, rather than addressing specific national or lo-

cal circumstances. Reviewers should be particularly careful to bear in mind that different people might make different decisions based on the same evidence. A good starting point for the discussion section of a review is to address any important methodological limitations of the included trials and the methods used in the review that might affect practical decisions about healthcare or future research. It is often helpful to discuss how the included studies fit into the context of other evidence that is not included in the review. Because conclusions regarding the strength of inferences about the effectiveness of an intervention are essentially causal inferences, reviewers might want to consider guidelines for assessing the strength of a causal inference e.g. how good is the quality of the included trials? How large and significant are the observed effects? How consistent are the effects across trials? Is there a clear dose-response relationship? Is there indirect evidence that supports the inference? Have other plausible competing explanations of the observed effects (e.g. bias or co-intervention) been ruled out?

Users of Cochrane Reviews must decide, either implicitly or explicitly, how applicable the evidence is to their particular circumstances. To do this, they must first decide whether the review provides valid information about potential benefits and harms that are important to them. To the extent that this is the case, they then need to decide whether the participants and settings in the included studies are reasonably similar to their own situation. In addition, it will often be important for them to consider the characteristics of the interventions or additional care provided in the included studies in reaching conclusions about the applicability of the evidence.

Issues of biologic variation that might be considered include divergence in pathophysiology (for example, biologic differences between women and men that are likely to affect responsiveness to a treatment) and divergence in a causative agent (e.g. for infectious diseases such as malaria). For some healthcare problems, such as psychiatric problems, cultural differences can sometimes limit the applicability of results.

Variation in the compliance of the recipients and providers of care

can limit the applicability of results. Predictable differences in compliance can be due to divergence in economic conditions or attitudes that make some forms of care not accessible or not feasible in some settings; for example, in developing countries.

The net benefit of any intervention depends on the risk of adverse outcomes without intervention, as well as on the effectiveness of the intervention. If there are no compelling reasons to assume that the relative benefits and harms are applicable, it is possible to estimate the expected impact of an intervention (e.g. the number needed to treat) by applying the estimated relative effect (e.g. relative risk) of an intervention to a specific baseline risk.

In addition to identifying limitations of the applicability of the results of a review, reviewers should discuss and draw conclusions about important variation in results within the circumstances to which the results are applicable. These might include: patient features, such as age, sex, biochemical markers; intervention features, such as the timing or intensity of the intervention; disease features, such as hormone receptor status

It can be helpful for reviewers to discuss the results of a review in the context of other relevant information, such as epidemiological data about the magnitude and distribution of a problem, information about current clinical practice from administrative databases or practice surveys, and information about costs. It must be kept in mind that evidence about the effects of healthcare is essential for well-informed decisions, but it is not sufficient.

In addition to considering the strength of evidence underlying any conclusions that are drawn, reviewers should be as explicit as possible about any judgements about preferences (the values attached to different outcomes) that are made. Health care interventions generally entail costs and risks of harm, as well as expectations of benefit. Drawing conclusions about the practical usefulness of an intervention entails making trade-offs, either implicitly or explicitly, between the estimated benefits and the estimated costs and harms.

Taking into account the above cautions about drawing conclusions, review groups and users of Cochrane Reviews, may find it useful to categorise interventions into exclusive categories, e.g. forms of care for which there is sufficient evidence to provide clear guidelines for practice, and forms of care for which the evidence is insufficient to provide clear guidelines for practice, but which should influence priorities for research. A common mistake that occurs, both in describing results and in reaching conclusions, when there is inconclusive evidence is to confuse 'no evidence of effect' with 'evidence of no effect'. A second common mistake is to reach conclusions that go beyond the evidence that is reviewed and statements like "more research is needed" should also be avoided. Reviewers should state exactly what research is needed and why. Opinions on how the review might be improved with additional data or resources can also be noted. Systematic consideration of the issues outlined above can guide the interpretation of the results of a review and help reviewers to avoid making incorrect or misleading inferences (Mulrow and Oxman 1997i).

4.4.6.1 Commentary: A good starting point for the discussion was to address any important methodological limitations of the included trials and the methods used. There is little doubt that this review was limited by the lack of good quality randomised placebo controlled trials with only six out of sixty-eight studies suitable for inclusion in the final meta-analysis. The quality of each study was assessed and a quality rating index calculated as described in the methods section of the review in order to help assess the strength of the inferences about the effectiveness of ALTENS/TENS in chronic low back pain. These six studies presented multipathology low back pain subjects, including many failed back surgery patients, used different trial methodologies and outcome assessments, a diverse follow-up - mostly for a short time only, and varied in quality and strength but nonetheless their assessment represented the best available evidence at this time for a systematic review. Moreover, these six studies also fit into the overall

context of the positive effects of ALTENS/TENS treatment for chronic low back pain, seen in the weaker uncontrolled evidence in the sixty-two studies not used in the meta-analysis. An experimental meta-analysis was performed (also see Appendix B (iv)) using the uncontrolled data and this is shown in comparison with the controlled data below. The table shows a comparison of the odds ratios (OR) of the meta-analysis of randomised controlled trials with an experimental and weighted meta-analysis of non-randomised trials and a standard placebo effect (derived from the average placebo effect of the six randomised controlled trials = 36%). It is interesting that this less powerful, and usually dismissed uncontrolled evidence, when pooled against the placebo responses obtained from the controlled trials, shows the expected higher odds ratios (apart from the ALTENS which sees a fall) typical from uncontrolled evidence, but nevertheless a distinctively similar trend response which may be worthy of further investigation in the future. We cannot of course ignore the anecdotal and unpublished clinical evidence, from the many patients who have benefited from these techniques or that of the practitioners, especially experts in the field, who administer these techniques, on a daily basis, and who see the beneficial effects in both the short and the long term.

Meta-analysis of TENS/ALTENS for pain relief	Odds ratios of randomised controlled trials of TENS/ ALTENS vs. Placebo	Odds ratios of non- ran- domised controlled trials of TENS/ ALTENS vs. Estimated standard pla- cebo in an experimental design
All trials of TENS and ALTENS	OR 2.1 (95% CI 1.3, 3.4) n = 288	OR 2.9 (95% CI 2.6, 3.2) n = 5652
Trials of ALTENS only	OR 7.2 (95% CI 2.6, 20.0) n = 61	OR 4.7 (95% CI 3.0, 7.2) n = 344
Trials of TENS only	OR 1.5 (95% CI 0.9, 2.6) n = 227	OR 2.7 (95% CI 2.4, 3.0) n = 4720

Figure XX: Table of comparisons - controlled vs uncontrolled meta-analyses

This Cochrane Review and meta-analysis, albeit based on only six studies and only 288 subjects shows a positive beneficial effect of using ALTENS/TENS in the treatment of chronic low back pain subjects at least in the short term. However, it is not possible to draw conclusions on the long-term benefits or otherwise of ALTENS/TENS treatments due to the lack of data to support it. The only study which gave a long term follow-up (Marchand 1993) showed no differences at three or six months but the quality of their study was only rated at .57 i.e. in the lower half of the six studies under consideration which weakens the strength of these conclusions somewhat. There were very few published negative trials and no unpublished negative or positive trials were identified as described in the text of the review.

Users of this Cochrane Review must decide on the applicability of the evidence presented for the use of ALTENS/TENS in the treatment of chronic low back pain. There seems little doubt that beneficial effects are obtained in the short-term treatment of multipathology chronic low back pain, including failed back surgery and with very little or no risk of adverse outcomes. There is, however, little evidence to confirm the long-term effects at this stage.

It is also important to consider the characteristics and responses to conventional TENS and Acupuncture-like TENS as identified in the table shown above. The use of additional care provided in the included studies in the form of exercise, analgesics and physical therapies such as heat must also be taken into account for evidence of any beneficial or unhelpful effects. The issue of biological variation does not appear to contribute greatly to this review e.g. biological differences between men and women, psychiatric problems, cultural differences or variation in compliance.

4.4.6.2 Conclusions: The magnitude and distribution of chronic low back pain on a global basis and the dearth of effective treatments confirmed by high quality randomised controlled trials creates an urgent need for systematic reviews of all clinical treatments in use for

this condition. The review under discussion is the first of many reviews currently under consideration and one which at last demonstrates that effective clinical benefits are to be found in the use of ALTENS/TENS for chronic low back pain, at least in the short term, this assessment being based on the best available evidence we have at this time (Spring 1998). Furthermore, it is an inexpensive and cost effective therapeutic measure with very few adverse outcomes. There may be inconclusive evidence on the long-term beneficial effects i.e. 'no evidence of effect' at this stage in our knowledge rather than there being 'evidence of no effect'.

This review goes on to suggest a way forward in the form of a definitive research study to confirm, strengthen and consolidate the last twenty-five years of research – once and for all as described in the conclusion section of the review which now follows. This is necessary in order to move the interventions of ALTENS and TENS on from 'the category of care for which there is insufficient evidence to provide clear guidelines for practice' to 'forms of care for which there is sufficient evidence to provide clear guidelines for practice'.

4.5 The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain. A Cochrane Review (Gadsby and Flowerdew 1997)

4.5.1 Introduction

This section of the thesis consists of the complete, original and latest version of the Cochrane Review (January 1998) as text extracted from the Cochrane Collaboration RevMan software into the Word97 format of this thesis, prior to submission of the original text to the Editorial Committee of the Back Subgroup for entry into ModMan and then on to the Cochrane Library for inclusion in the next CD-ROM edition (1998, Issue 2).

Also included in RevMan formats, are the 'Table of included studies', 'Table of excluded studies' and 'Metaview™' software charts - which are not reformattable into the thesis style of Microsoft Word 97. Metaview software is incorporated into RevMan and calculates the statistical analyses and prepares tabular and graphical displays of the results of the studies included in this review.

The Metaview charts display a summary, which includes the Peto Odds Ratio for the five comparisons plus individual charts for the following and a cumulative met-analysis for comparisons 1 and 3:

1. Comparison 1. TENS vs. Placebo in pain reduction
2. Comparison 2. ALTENS vs. Placebo in pain reduction
3. Comparison 3. TENS/ALTENS vs. Placebo in pain reduction
4. Comparison 5. ALTENS vs. Placebo and change in Range of Motion
5. Comparison 10. TENS/ALTENS vs. Placebo - treatment side effects.

4.5.2 The Cochrane Review

(Extracted from The Cochrane Library Issue 1 1998).

Title: The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain.

Short Title: TENS/ALTENS effectiveness in chronic low back pain

Abstract:

Objectives: To determine the effectiveness of transcutaneous electrical nerve stimulation in reducing pain and improving function in patients with chronic back pain.

Search Strategy: Electronic searches of EMBASE, MEDLINE, CISCOM, AMED for all studies of TENS treating chronic back pain together with citation tracking.

Selection Criteria: The inclusion criterion for studies included in this review, 6 out of 70 (at 1998), was comparisons of TENS/ALTENS versus placebo in patients with chronic back pain.

Data Collection and analysis: Outcome data on pain reduction, range of movement, functional and work status and trial design qualities was extracted by two reviewers.

Main Results: The ratio of odds of improvement in pain for each comparison was calculated: TENS/ALTENS vs. placebo at 2.11 (95% CI 1.32, 3.38) times that of placebo, ALTENS vs. placebo at 7.22 (95% CI 2.60, 20.01) and TENS vs. placebo at 1.52 (95% CI 0.90, 2.58). The odds of improvement in range of motion on ALTENS vs. placebo was 6.61 times (95% CI 2.36, 18.55) that of placebo.

Conclusions: There is statistically significant evidence, from the limited data available, that TENS/ALTENS reduces pain and improves range of motion in chronic back pain patients, at least in the short term. There is statistically significant evidence, pooling the TENS/ALTENS data in a cumulative meta-analysis, to indicate that using TENS/ALTENS for the treatment of chronic back pain in the short term, could have been shown to be beneficial almost 20 years ago. A powerful RCT of ALTENS and TENS is now needed to confirm these findings.

Background:

Practitioners specialising in musculoskeletal diseases are fully aware that the most common complaint world-wide is chronic low back pain and comprises the largest illness group in people of working age. The frequency of this complaint stands in contrast to the significant lack of understanding of its effective treatment and prognosis (Mooney and Cairns 1978) and attempts to decrease its impact by different educational, ergonomic or treatment methods have generally failed (Nachemson 1983). The diagnosis of low back pain remains a difficult conundrum. Pain syndromes are given many names in an attempt to describe what is probably most appropriately termed non-specific lumbar pain with and without radicular referral. The name used reflects the background, training, speciality and bias of the examiner. Some commonly used terms include lumbar sprain, lumbar strain, lumbago, myofascial pain, ilio-lumbar ligament syndrome, sacro-iliac dysfunction, lumbar misalignment and multifidus syndrome (Saal and Saal 1991). The National Back Pain Association UK also includes muscle spasm, prolapsed intervertebral discs, spinal stenosis, ankylosing spondylitis, facet joint degeneration, spondylosis, "failed back syndrome", osteochondritis, osteoporosis and degenerative disc diseases. Sweetman and colleagues have recently identified seven common patterns of low back pain and tests that would best help to recognise these different patterns (Sweetman 1992). It seems likely

that specialists will never agree which syndromes to recognise unless there is some ability to distinguish different patterns/sub-diagnoses of back pain. Studies on unselected mixed groups of different sorts of back pain are generally liable to fail to give any useful information and the ability to distinguish different patterns of back pain could make the difference between making valuable findings and failing to find conclusive evidence as has been so common in the past (Sweetman 1992).

In the United Kingdom, at least 1 in 5 people will suffer from low back pain during their lifetime and by 1991, the number of working days lost per year had risen from 57 million days at an estimated cost of £2 billion (Breen 1993) to 116 million days by 1995 at a cost of at least £5.1 billion (NBPA 1996). By 1995 back pain accounted for 14 million GP consultations, resulting in direct costs to the NHS of about £480 million and indirect costs to the country of £5 billion (Campbell 1995). It is estimated that 30% of adults become chronic sufferers but only 1% of back pain investigation results in surgery. There were 24,000 operations in 1993 in the UK alone (NBPA 1996).

In the United States, low back pain, often of a chronic nature, results in expenditure of at least \$13 billion a year for medical care (Deyo 1990). Early rehabilitation and a prompt return to work is important for stemming the economic drain that results from chronic disability. The development of cost-effective strategies for returning the patient to optimal levels of functioning as rapidly as possible has remained a therapeutic challenge (Herman 1994). A number of simultaneous treatments are usually advocated for patients with chronic low back pain, but few of these mixtures of treatments have ever been subjected to rigorous clinical evaluation.

Transcutaneous electrical nerve stimulation (TENS), originally based on the gate-control theory of pain (Melzack & Wall 1965), is

widely used for the treatment of low back pain. Despite its wide use and theoretical rationale, there is meagre scientific evidence at this stage to support its use, this based on the controlled trials of the efficacy of TENS in treating chronic back pain up to 1990 (Deyo 1990). Transcutaneous electrical nerve stimulation (TENS) is also known as conventional high frequency, low intensity TENS and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) is also known as low frequency, high intensity TENS. Transcutaneous electrical nerve stimulation (TENS), is based on and explained by, the gate-control theory of pain and uses frequencies of stimulation above 10pps (pulses per second or Hz) but usually between 80-100pps. Acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) is based on the mode of traditional acupuncture needle stimulation which is less than 3 pulses per second (usually 2pps) and the presumed working mechanism of the endorphin response. The use of conventional TENS treatment appears to produce rapid pain relief, due to pre-synaptic inhibition of pain messages with the instantaneous release of GABA by the large fibres, during the times of stimulation. This response usually ends on termination of the treatment. ALTENS is said to produce enduring pain relief, by pre-synaptic and post-synaptic endorphin controlled pain inhibition plus pituitary endorphin release, following the treatment session (Pomeranz 1987, 1990, 1995) and there is evidence to support the cumulative effects of ALTENS treatment over a period of time (Pomeranz 1987, 1990, 1995; Cheing 1996). These two methods for chronic low back pain management have experienced a tremendous growth over the past 25 years. The TENS literature, demonstrating both positive and negative results, has been subjected to extensive narrative reviews (Shealy 1974; Long 1991; Shealy and Mauldin 1994). It was suggested over 20 years ago that TENS had a potentially important role in acute and chronic pain management and that large numbers of pain patients should benefit from this approach (Shealy 1974). There has been many trials of TENS and ALTENS for pain control since then with over 600 publications

(Nolan 1991) supporting its efficacy, claiming at least 50% pain relief in chronic back pain patients (Shealy 1994). There have been other trials (e.g. Deyo 1990) which have refuted this effectiveness. A recent Dutch review of three trials, in a systematic mega-review, concluded that "there is no evidence that TENS is an effective treatment for chronic low back pain because of the contradictory results of the two high quality studies" (van Tulder 1996) and a Canadian Health Technology Assessment concluded that TENS had not undergone a sufficiently strict and rigorous clinical evaluation and that few reports met acceptable scientific criteria (Reeve 1995) to which the authors of this review would agree. However, the Canadian assessment is also an overview of several TENS applications and is based on a small and limited number of studies (TENS and chronic low back pain = 10 studies). This Systematic Review and meta-analysis examines just one application of TENS to chronic low back pain in more detail and reviews seventy studies. However, there are only six RCT's which in the opinion of the authors truly provide efficacy data out of the 70 studies on chronic low back pain which were identified during the search strategy. These 70 studies are a subset of more than 600 publications (covering all clinical applications of TENS/ALTENS and other electrostimulation techniques) identified by Nolan (1991) together with the subsequent publications from the period 1991-1997. If TENS and ALTENS can be shown to be therapeutically effective and cost-effective, using the techniques of Systematic Review, within the framework of The Cochrane Collaboration, then the potential scale of their use worldwide would be enormous.

Objectives:

To determine the effectiveness of transcutaneous electrical nerve stimulation as conventional TENS and Acupuncture-like TENS in achieving pain reduction, improving range of movement (ROM), improving functional status and return to work in patients with chronic low back pain. This is necessary, in view of the numerous conflicting

studies and reviews recently undertaken in this area, in order to provide a clearer assessment using a systematic review and meta-analysis, so that patients and practitioners are able to make a more informed choice in respect of either using or rejecting these increasingly popular treatments.

We will test the following hypotheses:

1. The use of TENS treatment for chronic low back pain is more effective than placebo for reducing pain (Comparison 1).
2. The use of ALTENS treatment for chronic low back pain is more effective than placebo for reducing pain (Comparison 2).
3. The use of TENS/ALTENS treatment for chronic low back pain is more effective than placebo for reducing pain (Comparison 3).
4. The use of TENS treatment for chronic low-back pain is more effective than placebo for improving range of movement (Comparison 4).
5. The use of ALTENS treatment for chronic low back pain is more effective than placebo for improving range of movement (Comparison 5).
6. The use of TENS/ALTENS treatment for chronic low back pain is more effective than placebo for improving range of movement (Comparison 6).
7. The use of TENS treatment for chronic low back pain is more effective than placebo for improving functional status and return to work (Comparison 7).
8. The use of ALTENS treatment for chronic low back pain is more effective than placebo for improving functional status and return to work (Comparison 8).
9. The use of TENS/ALTENS treatment for chronic low back pain is more effective than placebo for improving functional status and return to work (Comparison 9).
10. The use of TENS/ALTENS treatment for chronic low back pain is relatively free from side-effects in comparison to a placebo (Comparison 10).

Selection criteria - types of studies

All randomised controlled comparisons of TENS or ALTENS therapy versus placebo in the rehabilitation of patients with chronic low back pain have been included.

Selection criteria - types of participants

Patients of either gender with chronic low back pain, irrespective of the specific local diagnosis, and with a history of at least 8 weeks duration were included.

Selection criteria - types of interventions

The electrotherapeutic techniques of conventional high frequency low intensity TENS and/or low frequency high intensity ALTENS versus a credible placebo control. The inclusion/exclusion criteria for studies in respect of the stimulation modes were based on the electrical parameters described by Mannheimer and Lampe (1984), Robinson (1996) and Walsh (1997):

- a. Conventional TENS using a high rate, narrow pulse and moderate stimulation with parameter adjustments for rate between 50 to 100Hz and a low pulse width from 40-75 microseconds and an intensity raised to the level of comfort.
- b. Acupuncture-like TENS (also known as "strong low rate (SLR) TENS - Robinson 1996) with electrical parameters adjusted to provide a low rate (1 to 4Hz), a wide pulse width between 150 to 250 microseconds and an intensity at as high a level as tolerated by the patient.
- c. Other less used and little researched modes such as subsensory stimulation, noxious level stimulation, burst train and modulated forms of electrical stimulation were not included in this review.

Selection criteria - types of outcome measures

The types of outcome measures considered in this review were as follows:

- i. initial effectiveness was assessed in terms of an overall improvement in the levels of pain as measured by an appropriately validated clinical pain intensity rating method (Jensen 1986).
- ii. an improved level of range of movement (ROM) using a suitable validated ROM procedure e.g. straight-leg raising, spinal and hip flexion assessments and Schober's spinal flexion assessment (Bluestone 1985).
- iii. an assessment of functional status and well-being as an increasingly advocated goal in the treatment of patients with chronic conditions (Stewart 1989) e.g. the modified Sickness Impact Profile validated for use in low back pain (Follick 1985).
- iv. a return to work by an early, gradual, biomechanically controlled return for those subjects in whom no objective cause for the pain can be found after thorough examination (Nachemson 1983)
- v. with follow-up assessments of both pain and activity improvements and
- vi. an assessment of the incidence of side-effects.

An improvement would be recorded if a total or partial relief of pain or increased activity level were experienced. Non-improvement would be recorded if no decrease in pain or ROM rating occurred at the end of the initial course of treatment and at follow-up. An assessment of an improvement in functional status using an appropriate validated tool together with a return to work would also be made.

Exclusion Criteria

All randomised controlled trials which failed to compare an active TENS or ALTENS treatment with a credible placebo treatment, failed to meet the high frequency (>10Hz) low intensity parameters of conventional TENS or low frequency (<3Hz) high intensity parameters of ALTENS in the treatment of chronic low back pain were excluded from this review.

Search strategy for the identification of studies

Primary research:

- (a) MEDLINE (1966 to November 1997), EMBASE (1985 to September 1995) AMED and CISCOR (from database start date to January 1995) were searched using the terms Transcutaneous Electrical Nerve Stimulation or TENS/ ALTENS, Transcutaneous Nerve Stimulation or TNS, Transcutaneous Electrical Neurostimulation or TENMS, Electroacupuncture, Transdermal Electrical Stimulation, [Peripheral] Conditioning Stimulation or [P]CS, Percutaneous Neural Stimulation, Microamperage Electrical Stimulation or MENS, Cranial Electrotherapy Stimulation or CES, Transcutaneous Cranial Electrical Stimulation or TCES, Transabdominal Neurostimulation or TANS (after Nolan 1991) in order to identify all studies of electrostimulation in the English language (no studies in languages other than the English language were identified during these searches but ongoing searches for these studies continues). Obvious non-low back pain studies were eliminated and the rest of the studies were then searched by hand for those meeting the criteria of the review. An initial pilot search of the MEDLINE database using the above search phrases, plus the recommended Cochrane CMSG search phrase strategy for controlled trials, and back pain had identified only a small number of studies ($n = 3$);
- (b) Searching the reference lists of these trials and citation tracking to identify possible studies missed by the computerised search;
- (c) Searching books related to Transcutaneous Electrical Nerve Stimulation, physical therapies and acupuncture/ electroacupuncture techniques;
- (d) Searching published abstracts from pain and Orthopaedic conferences;
- (e) Conversation with colleagues (particularly those who have co-ordinated such studies and those who have their own database of trials, e.g. Database Field Physical Therapy and Rehabilitation, University of Limburg - to September 1995; MWF Listings, Beccles, UK. to July 1995);

(f) Sending letters to major investigators of TENS and ALTENS techniques seeking information on published and unpublished trials and asking them to check that the list of references was indeed comprehensive;

(g) Narrative review articles and their reference lists.

UPDATE 1998:

Critics of this review have pointed out the lack of non-English language studies included in the review albeit Gemignani's (1991) study originated from Italy and Marchand (1993), a French Canadian study, and both were included in the six studies included in this review. Studies not meeting the inclusion criteria and excluded from this review included those studies published in the English language but originating from Sweden (5), Italy (2), Finland (2), The Netherlands (2), Poland (1), India (1), Nigeria (1) and Saudi Arabia (1). The bibliographies of these papers were again checked (Jan 1998) for non-English language placebo controlled RCT studies but no more new studies were identified.

Moreover, in the light of these comments and criticisms the search strategy was repeated again, in December 1997, as described above, together with a specific search strategy to identify non-English language publications of randomised controlled trials of TENS/ALTENS with special attention directed to the European EMBASE database. This search identified 71 studies on TENS/ALTENS in languages other than English. These studies covered many applications for pain but none were identified for chronic (or acute) back pain.

Through the CCINFO (Cochrane Collaboration Information mailing list) members of the Collaboration in 23 countries were also circulated with a request for help in identifying non-English language publications. Two Italian studies were suggested (Zelaschi et al (1982

and Coli et al 1992) and these studies were translated and reviewed by Elena Telaro, Research assistant with the Italian Cochrane Centre, Milano, Italy. Unfortunately, neither of these two studies met the inclusion criteria for this review - one study (Zelaschi 1982) did not contain any LBP subjects at all and the second (Coli 1992) was not a placebo controlled RCT.

The authors suggest that at this moment in time (January 1998), this review appears to contain all the studies identifiable within the research strategy as described above.

Methods of the review

Selection of Trials

The inclusion criteria were liberally applied in deciding which articles to retrieve. Seventy studies were identified and collected. Two reviewers (JGG, MWF), both content area experts, independently evaluated the trials to be included in the review. The names of the authors, institutions, journal of publication and results were known to the reviewers following the guidelines of Blair (1995) as blinding would have made it difficult to recognise the multiple publications of the same study rather than individual studies. The decision rule for disagreements was resolved by discussion. A pilot assessment was carried out on three studies to refine and clarify the data collection tools, based on Vickers 1995, and to evaluate the reliability of the inclusion/exclusion criteria. This was followed by the full review. One of us (JGG) sought additional information for all randomised, controlled trials that appeared to meet the inclusion criteria. A single reviewer JGG co-ordinated the final reviews. Six studies meeting the inclusion criteria were reviewed and sixty-four studies were excluded. Of these sixty four excluded trials, forty were reviewed in more detail to assess methodological and statistical data, as some of these studies had been included in other reviews but were subsequently excluded from ours

(see 'Description of studies' section and also tables of included and excludes studies extracted from RevMan which are found at the end of this section 4.5).

Quality Assessment

The quality of the methodology of each of the selected studies was initially rated using the Cochrane Collaboration guidelines (Sackett 1994) and the following criteria of quality were assessed using the above methodology:

1. adequate allocation concealment:

A = adequate concealment: some form of centralised, randomisation scheme via office by phone to receive the treatment allocation; an on-site computer system with access only after inputting the characteristics of an enrolled participant; by assignment envelopes, sequentially numbered, sealed and opaque; other methods that ensure adequate concealment.

B = unclear concealment: stating that a list or table was used for assignment; just specifying that envelopes or sealed envelopes were used; any other unclear allocation scheme.

C = inadequate concealment: alternation; reference to case record numbers, dates of birth, day of the week or similar approach; any allocation procedure that was entirely transparent before assignment, such as an open list of random numbers.

2. Other components of trial quality considered in this review were:

a) double-blinding: was the study described as double-blind, bearing in mind the perennial problems in making trials involving physical treatment double-blind?

b) control/ placebo intervention: were the physical characteristics of the control/ placebo intervention credible?

c) pain and/or activity assessments: were the assessment techniques valid e.g. a validated pain or range of movement activity assessment method? Was the level of activity assessed subjectively or objectively? Were general measures of functional status and well-being assessed

together with perhaps the single most effective manoeuvre that reduces pain - the return and absorption by the patient in work (Wynn Parry 1980 in Nachemson 1983)?

d) withdrawals after randomisation: were the numbers of drop outs and withdrawals identified in the study report and how were they handled?

3. In addition, the six randomised controlled trials meeting the inclusion criteria for this systematic review and meta-analysis were rated for experimental design quality using the Reeve's 1995 scale, which is a modification of a scale originally published by Chalmers (1981), as the design of the clinical trial is considered the most important part of a RCT (Chalmers et al. 1981). See 'Methodological quality' section for more details.

4. On completion of the quality assessment form for each of the six studies, an index of experimental design quality for each RCT was then calculated, (after Chalmers 1981), by dividing the total score obtained by the total possible score, normally 60 but 57 for this review, because the compliance section was not applicable in this instance with all treatments administered on site by health care practitioners.

5. The quality of all the trials that met the inclusion criteria were assessed in accordance with the explicit criteria identified above and the quality assessments so determined were used as weighting in the Revman analysis and are also identified in the 'table of included studies'.

Management of Withdrawals

In most reported trials, a number of patient's drop out or are withdrawn after the trial is underway. The number of drop outs, their details and statistics for each trial group was assessed by the reviewers e.g. were the drop outs listed by diagnosis, treatment and reason for withdrawal and whether withdrawal occurred as a result of patient or investigator initiative, what percentage of the group was involved? How were they handled? For different kinds of withdrawals could bias

the final composition of each treatment group, thus diminishing the efficacy of the randomisation procedure for obtaining similar kinds of patients in each treatment group. In this category, RCT's that do not mention withdrawals or whose withdrawals exceed 10% in the case of patients followed up for 3 months or less, or whose withdrawals exceed 15% for longer than 3 months follow up were carefully scrutinised (Chalmers 1981).

Data Management

The two reviewers applied the following guidelines to re-analyse data from the studies selected:

- (a) The analysis included all subjects who completed the trial and maintained the study groups according to the original randomisation procedure.
- (b) Data regarding the study populations, interventions, numbers with each outcome event (i.e. improved pain control, range of movement and functional status, and return to work) and side effects by allocated treated group, quality measures and the results were extracted using a 'reviewers check list' and a 'characteristics of trials contributing to the review sheet' (also see Appendix B (ii)).
- (c) If any of the above information was not available in the publications, it was sought by correspondence with the trial authors (by JGG).

The reviewers agreed upon these rules during the protocol development stage and before knowing the number or quality of the studies selected.

Model Validity

The concept of model validity is extremely important in the assessment of physical therapies, surgery and many complementary therapies in which, for example, the competence of practitioners (in the study) can affect its result. Since a negative result may reflect the inadequacy of the practitioner rather than the inefficacy of the tech-

nique, a trial should state the training and professional standing of the practitioners involved. Other aspects of model validity include an assessment of the adequacy of the intervention, the number of practitioners involved and treatment realism i.e. is the treatment like that used in everyday practice? (Vickers 1995). The model validity of each trial in this review was assessed by the reviewers and is shown in the 'table of included studies' at the end of this section.

Methods used to synthesise the data:

The systematic review and meta-analysis were made on the database of studies comprising randomized controlled studies, blind and unblind studies and studies of varying power. Each included trial used a different clinical scoring system for assessing outcome. Most studies looked at the numbers of subjects with an improvement in the outcome assessed, others at changes in the mean scores of a rated outcome. We used numbers of subjects showing a clinical improvement in an outcome and those studies with mean scores were converted to this mode.

(a) A weighted estimate of the typical treatment effect across the six studies "the typical odds ratio" (i.e. the ratio of odds of a favourable outcome among treatment-allocated patients to the corresponding odds among the control group), calculated using the standard "fixed-effects" method of Peto, with the respective 95% confidence intervals (CI) around this.

(b) We tested for heterogeneity between trial results using a standard chi-squared test on N degrees of freedom where N equals the number of trials contributing data minus one.

Description of studies

The six studies meeting the inclusion criteria for this review and meta-analysis can be regarded as fairly comparable in relation to the inclusion/exclusion criteria as applied by the reviewers with two

ALTENS, three TENS and one mixed frequency (ALTENS and TENS) study.

Description of Patient Selection Criteria:

The total number of chronic low back pain subjects in the 6 studies was 288 and an average age range of 45-50 years with approximately equal numbers of women and men.

Severity and duration of illness:

All subjects had chronic low back pain for at least 8 weeks, but most of them had a history of several years, and constituted the most severe cases which had not responded to the usual orthodox and alternative interventions. The study of Deyo 1990 included patients with non-specific diagnoses for low back pain and 34% were post-surgery patients. The study of Thorsteinsson 1977 included patients with non-specific diagnoses for low back pain and 90% were post-surgery patients. The study of Melzack 1983 included patients with non-specific diagnoses for low back pain and no details of previous surgery. The study of Marchand 1993 included patients with ankylosing spondylitis and rheumatoid arthritis as well as non-specific low back pain. The study of Gemignani 1991 included only ankylosing spondylitis patients with low back pain. The study of Jeans 1979 included patients with non-specific diagnoses for low back pain.

Cultural setting:

Studies were conducted in Canada, Italy and the USA.

Descriptions of Interventions:

1. ALTENS studies, Melzack 1983 and Gemignani 1991 used pulse frequencies between 4 and 8Hz for 20-30 minutes for 5-10 treatments.
2. TENS studies, Marchand 1993, Thorsteinsson 1977 and Jeans 1979 used pulse frequencies between 15 and 180Hz for 20-30 minutes for 3-20 treatments

3. One study, Deyo 1990 used either 80-100Hz TENS or 2-4Hz (ALTENS) for 45 minutes for up to 42 treatments.

4. All studies used a credible placebo control.

Description of Study Design:

All trials were described as 'randomised' and all but Marchand 1993 were described as double-blind - see Methodological Quality section for further details.

Outcomes:

(i) Definition of improvement/non-improvement:

An improvement would be recorded if a total or partial relief of pain, or increased range of movement/ROM activity, or improvement in functional status or return to work were experienced. A non-improvement would be recorded if there was no decrease in pain, ROM or functional status ratings, or return to work, occurred at the end of the initial course of treatment and follow up.

(ii) Measurement:

For outcomes that involved measurement of pain, the McGill Pain Questionnaire (Melzack 1983, Jeans 1979), Visual Analogue Scales (Gemignani 1991, Marchand 1993, Deyo 1990), a Numerical Rating Scale (Thorsteinsson 1977) were used. For outcomes that involved measurement of range of movement or activity, straight leg raising (Melzack 1983, Deyo 1990), back flexion (Melzack 1983) and Schober's test, finger-to-floor distance in anterior and lateral flexion (Gemignani 1991, Deyo 1990) were used.

(iii) Duration of follow up:

No follow up (Melzack 1983, Gemignani 1991 and Jeans 1979), up to 2 months (Deyo 1990) and up to 6 months (Marchand 1993 and Thorsteinsson 1977).

See the 'table of included studies' at the end of 4.5 for more details.

Reasons for excluding studies

1. All randomised controlled trials, which failed to compare an active conventional TENS or acupuncture-like TENS with a credible placebo treatment.
2. All studies which failed to meet the recognised electrical parameters for high frequency ($>10\text{Hz}$) low intensity parameters of conventional TENS or low frequency ($<4\text{Hz}$) high intensity stimulation of ALTENS (also known as "strong low rate (SLR) TENS) in the treatment of chronic low back pain.
3. All other studies which described less used and little researched modes of transcutaneous electrical nerve stimulation such as sub-sensory stimulation, noxious level stimulation, burst train and modulated forms of electrical stimulation.
4. Studies were also excluded if they reported on acute (six weeks or less) low back pain patients or studies with a mix of acute and chronic low back pain patients.
5. All uncontrolled and non-randomised studies of TENS/ALTENS and chronic back pain.
6. All descriptive studies of TENS and chronic low back pain.

Forty-two studies lacked random assignment and/or an appropriate control group and 22 descriptive studies were excluded. Included in this total of sixty-four studies were the following studies, which had been included in other reviews on TENS and chronic low back pain but were excluded from this review for the reasons, stated below:

Lehmann 1983 and Lehmann 1986 (a repeat of Lehmann 1983):

This was a trial of subthreshold continuous TENS, electroacupuncture and a placebo group, which did not meet the electrical parameters for either TENS or ALTENS as described in this review. Few experimental details were given; patients were treated on an individual basis and not always given the same treatment; subjects were heavily selected

(for this trial); samples were not equal in size; no details of electrical parameters were given; no details of electrode placement; numbers of patients getting relief was not stated; data does not add up; with over complex and over reporting influencing outcome; finally subthreshold TENS had already been subjected to trial by Long 1979 and found to be no more effective than a unit with a dead battery.

Herman 1993:

This was a randomized controlled trial of a 'novel' transcutaneous electrical nerve stimulator called "CODETRON" which did not meet the electrical parameters of this review and furthermore was applied in a rehabilitation programme for acute occupational low back pain. The FDA would not permit sale of this unit before 1995 and it was classed as experimental (Pomeranz 1996).

Melzack 1980:

This was a cross-over design trial of continuous ALTENS as a standardised intervention vs. ice massage with no blinding, no baseline matching or group comparability; no inclusion/ exclusion criteria or concealed randomisation described; McGill Pain Questionnaire assessment of pain but no activity assessments. No credible placebo control treatment described (for this trial).

Fox 1976a/b

This was an uncontrolled cross-over trial of TENS vs. acupuncture as a standardised intervention with no randomisation, blinding, baseline matching, inclusion/exclusion criteria or washout period described. No credible placebo control treatment described (for this trial).

Pope 1994:

This was a comparative trial of 4 treatment groups for low back pain as manipulation; a modulated burst transcutaneous muscular stimulation (TMS), massage and corset. This was a high frequency,

high intensity electrical stimulation that did not meet the electrical parameters of this review for either TENS or ALTENS.

Long 1979:

This was an uncontrolled study of TENS following on from Long (1974 - also see Long 1975) with no details of electrode placements, electrical parameters, standardisation of intervention, randomisation, blinding techniques or inclusion/ exclusion criteria.

Loeser 1975:

This was an uncontrolled trial of TENS with no standardisation of the treatment intervention, randomisation, blinding, no description of outcome measures used, no details of inclusion/ exclusion criteria or details of baseline matching or group comparability.

Procacci 1977:

This was an uncontrolled trial of continuous TENS as a standardised intervention with no details of randomisation, matching, blinding, inclusion/exclusion criteria, or details of outcome measures except for the clinical examination.

Macdonald 1983:

This was a placebo controlled trial of superficial acupuncture (4mm depth) vs. placebo for chronic low back pain and was therefore not a trial of TENS or ALTENS.

See 'table of excluded studies' at the end of 4.5 for more details.

Methodological quality of included studies

Each trial in this review was the subject of a quality rating as described under 'Methods of the review' (also see Appendix B (iii)) and further details, quality scores, general quality characteristics and flaws in the individual trials are described below. We used the Reeve

et al. 1995 Quality Rating Scale in this review, a modified scale first used in a Technology Assessment of Transcutaneous Electrical Nerve Stimulation by the Canadian Co-ordinating Office for Health Technology Assessment and illustrated below in Figure XXI. Each trial is rated along a number of dimensions and a total score accumulated. The range of the scale is from 0 (low quality) to 60 (high quality). From the original 0 to 100 scale published by (Chalmers 1981), only the elements evaluating study design were used: selection and description of subjects, withdrawals and reasons for withdrawals, definition of therapeutic regime, use of placebo, blinding, randomisation, compliance and outcome measures. In addition, the scale was revised to include inclusion and exclusion criteria, and an indication whether the procedure of administering TENS and the placebo were identical. This modified scale has 16 elements (Reeve et al 1995) as shown below.

Figure XXI: Table - the Modified Chalmers et al. 1981 by Reeve et al. 1995 system for evaluating the methodological quality of a randomised controlled trial.

Item	Maximum Possible Points
1. Description of selection of subject was adequate	3
2. Description of patients screened was provided	3
3. Inclusion criteria for study included	1.5
4. Exclusion criteria for study included	1.5
5. Withdrawals and reason for withdrawal were described	3
6. Therapeutic regimen was defined	3
7. Appearance of TENS unit and placebo unit was identical	1.5
8. Procedure for administering TENS/ placebo was identical	1.5
9. Randomisation was blinded	10
10. Patients were blinded to treatment group	8
11. Practitioners were blinded to treatment group	8
12. Number of subjects needed in trial was estimated a priori	3
13. Adequacy of randomisation was evaluated	3

14. Adequacy of blinding was evaluated	3
15. Compliance with treatment was assessed	3
16. Measure of outcome of the active therapy was made	3
Total points possible	60

The Quality Index Rating for each of the six trials was then calculated by dividing the total score obtained by the total possible score of 57 (in this review) as shown in Figure XXII:

Trial	Quality Index (QI)
Deyo 1990	0.84
Thorsteinsson 1977	0.71
Melzack 1983	0.70
Gemignani 1991	0.59
Marchand 1993	0.57
Jeans 1979	0.55

Figure XXII: The Quality Index Rating Table for each of the six trials.

The general quality of the trials is summarized below and further details are included in the 'table of included studies'.

Deyo 1990: TENS/ALTENS vs. placebo (n=31 vs. n=31); (QI = 0.84)
This was a randomised controlled trial of TENS and/or ALTENS, was not described as double-blind, and scored the highest number of points of the six studies included in this review. The methodology in general is an excellent example for other researchers to follow. Description of subjects, screening, inclusion and exclusion criteria, withdrawals and their management, the therapeutic regimen, appearance and administration of TENS and placebo, the blinding of the randomisation process, blinding of patients, evaluation of randomi-

sation and outcome measures (11 indicators of pain, function, and back flexion) were well described and implemented.

Flaws in the study: The subjects were recruited by advert and heavily screened before the trial. Practitioners were not all blinded to the treatment groups, the numbers of subjects needed was not estimated a priori and the adequacy of blinding was only partially evaluated. The TENS intervention was not a standardised intervention and there were too many groups and variables, (e.g. exercise, moist heat packs and electric heating pads at home,) which caused difficulty evaluating the efficacy of the primary intervention and the credibility of the placebo control. The assumption that the effect of such heat treatment was exactly the same in each group is unverified. The question of pain evaluation may also be challenged because pain was measured for short periods (of time) only without considering pain modulation over time and context. There was a high withdrawal rate, above 14% in the first month and over 16% in the following two months even though this was handled satisfactorily at the analysis stage. The primary comparison of TENS vs. Sham TENS (n=31 vs. n=31) contained unequal numbers of post-surgery subjects (n=19 vs. n=10) which affects the baseline matching of subjects in this trial, albeit multivariate analyses was described. Pooling of the four different groups into two increased the ratio of post-surgery subjects to n=22 vs. n=20 in an attempt to adjust for base-line differences.

Thorsteinsson 1977: TENS vs. placebo (n=33 vs. n=33); (QI = 0.71)

This was a cross-over randomised controlled trial of TENS, described as double-blind, and scored the second highest mark in the review. Descriptions of subjects, inclusion criteria, therapeutic regimen, appearance and administration of TENS and placebo, the blinding of the randomisation process, blinding of practitioners were well described and implemented.

Flaws in the study: A cross-over trial between TENS and placebo TENS which would make blinding of patients virtually impossible after

the crossover, with no washout period and only three days of treatment before initial outcome evaluation but described an adequate follow up period. No exclusion criteria described, no estimation of subjects needed in trial a priori, only partial evaluation of adequacy of randomisation and blinding and measures of outcome was made. No details of withdrawals and handling given.

Melzack 1983: ALTENS vs. placebo (n=20 vs. n=21); (QI = 0.70)

This was a randomised controlled trial of ALTENS, described as double-blind, and scored the third highest mark in the review. Descriptions of subjects, therapeutic regimen, the blinding of the randomisation process, estimates of number of subjects needed in the trial and outcome measures were well described and implemented.

Flaws in the study: This study compared TENS with a gentle suction massage (which might just be classed as an adequate placebo treatment), a pair of treatments for which patients obviously could not be blinded as to study assignment. A partial description only of inclusion/exclusion criteria given, different TENS units and procedure for administration was described, practitioners were not all blinded to the treatment groups, only measured pain relief immediately following the treatment session and no follow up, the adequacy of randomisation and blinding was only partially evaluated. No details of withdrawals and handling given.

Gemignani 1991: ALTENS vs. placebo (n=10 vs. n=10); (QI = 0.59)

This was a randomised controlled trial of ALTENS and scored the fourth highest mark in the review. Descriptions of subjects, inclusion criteria, therapeutic regimen, appearance of TENS and placebo unit and administration of identical procedure, the blinding of the randomisation process and measures of outcome were well described and implemented. There were no withdrawals from the study.

Flaws in the study: no exclusion criteria described, partial blinding of patients and practitioners to treatment group, number of subjects

needed for trial not estimated a priori and adequacy of randomisation and blinding only partially evaluated.

Marchand 1993: TENS vs. placebo (n=14 vs. n=12); (QI = 0.57)

This was a randomised controlled trial of TENS, described as double-blind, and scored the fifth highest mark in the review. Descriptions of subjects and screening, inclusion and exclusion criteria, therapeutic regimen, procedure for administering identical treatment for TENS and placebo and blinding of patients to treatment group were well described and implemented,

Flaws in the study: Described as a randomised trial but in fact was a 'pseudo-random' trial and 'done controlling for four variables: sex, weight, diagnosis and pain severity'. The appearance of the TENS and placebo units were different, there was only partial blinding of the randomisation process and practitioners, no estimation of subjects needed in trial a priori, only partial evaluation of adequacy of randomisation and blinding and measures of outcome was made. No details of withdrawals and handling given.

Jeans 1979: TENS vs. placebo (n=6 vs. n=4); (QI = 0.55)

This was a randomised controlled trial of TENS and scored the sixth mark in the review. Descriptions of the therapeutic regimen, the procedure for identical administration of TENS and placebo and the blinding of patients to treatment group was well described and implemented. There were no withdrawals from the study.

Flaws in the study: A fair description of subjects selected was given, with a partial inclusion criteria for the study, different TENS and placebo units, partial blinding of the randomisation process, partial blinding of the practitioners to the treatment group, the number of subjects needed for the trial was not estimated a priori, the adequacy of randomisation and blinding was only partially evaluated and only partial measures of outcome of the active therapy was made.

Results

The six trials included in this review contained 288 subjects - a very small number considering the database of trials reviewed; 118 subjects in 4 trials were given TENS, 30 subjects in 2 trials were given ALTENS and 140 subjects in the 6 trials were given placebo treatments. The meta-analyses show an increase in the odds of improvement in pain and improvement in the range of movement as outlined below.

1. The use of TENS treatment for chronic low back pain is more effective than placebo for reducing pain (Comparison 1). TENS reduced the pain levels of chronic low back pain subjects with an OR of 1.52 times (95% CI 0.90, 2.58) more likely to show an improvement on TENS as compared to placebo in the four TENS trials in this review.
2. The use of ALTENS treatment for chronic low back pain is more effective than placebo for reducing pain (Comparison 2). ALTENS reduced the pain levels of chronic low back pain subjects with an OR of 7.22 times (95% CI 2.60, 20.01) more likely to show an improvement on ALTENS as compared to placebo in the two ALTENS trials of this review.
3. The use of TENS/ALTENS treatment for chronic low back pain is more effective than placebo for reducing pain (Comparison 3). TENS and ALTENS reduced the pain levels of chronic low back pain subjects with an OR of 2.11 times (95% CI 1.32, 3.38) more likely to show an improvement on TENS/ALTENS as compared to placebo in the six trials of this review.
4. The use of TENS treatment for chronic low back pain is more effective than placebo for improving range of movement (Comparison 4). There was insufficient data on TENS treatment alone to evaluate the range of movement in this group. Deyo 1990 included measures not only of straight leg raising, but also the Schober test and finger-to-floor measurements of range of movement but there were no clinically important or statistically significant differences in any of these out-

comes between the subjects receiving TENS and those receiving sham TENS.

5. The use of ALTENS treatment for chronic low back pain is more effective than placebo for improving range of movement (Comparison 5). ALTENS improved the range of movement by assessment with an OR at the end of the initial course of treatment of 6.61 times (95% CI 2.36, 18.55) more likely to show an improvement on ALTENS as compared to placebo in the two ALTENS trials of this review. Melzack 1983 assessed two ranges of movement tests - straight leg raising and back flexion and Gemignani 1991 assessed Schobers test and finger-to-floor distance in anterior and lateral flexion. In Melzack's study spinal flexion got worse in both the control and the TENS groups.

6. The use of TENS/ALTENS treatment for chronic low back pain is more effective than placebo for improving range of movement (Comparison 6) but there was insufficient data to evaluate the range of movement in this group further.

7. The use of TENS treatment for chronic low back pain is more effective than placebo for improving functional status and return to work (Comparison 7). There was insufficient data to evaluate the outcomes of functional status and well being and no data to evaluate return to work in the four TENS studies of this review. Deyo 1990 included measures to evaluate functional status using a modified Sickness Impact Profile but there were no clinically important or statistically significant differences in any of the outcomes assessed between the subjects receiving TENS and those receiving sham TENS.

8. The use of ALTENS treatment for chronic low back pain is more effective than placebo for improving functional status and return to work (Comparison 8). There was insufficient data to evaluate the outcomes of functional status and well being and no data to evaluate return to work in the two ALTENS studies in this review.

9. The use of TENS/ALTENS treatment for chronic low back pain is more effective than placebo for improving functional status and return to work (Comparison 9). There was insufficient data to evaluate fur-

ther the outcomes of functional status and well being and no data to evaluate return to work in the six studies in this review.

10. The use of TENS/ALTENS treatment for chronic low back pain is relatively free from side-effects in comparison to a placebo (Comparison 10). TENS and mixed TENS/ALTENS treatment both carried the risk of side effects described as mild (usually) skin rashes, worsening of pain or mild mental disturbances with an OR at the end of the initial course of treatment of 1.08 (95% CI 0.55, 2.11) among those trials which had reported side effects. No side effects were reported in the included ALTENS trials or for placebo treatments.

Sub-group analyses:

It was not possible to conduct any separate sub-group analyses on the above data. This included the responses of post-surgery patients vs. no surgery patients to TENS or ALTENS treatment due to lack of suitable data on their responses.

Basic statistics:

The total number of subjects given TENS was 118 with 54 (45.8%; 95%CI 37.0%, 55.0%) of subjects showing a positive response by the end of the trials. The total number of subjects given ALTENS was 30 with 26 (86.7%; 95% CI 80.0%, 93.0%) subjects showing a positive response by the end of the trials. The total number of subjects given TENS/ ALTENS and placebo was 288 with 131 (45.5%; 95% CI 39.6%, 51.3%) subjects showing a positive treatment response by the end of the trials. The total number of patients given placebo treatment was 140 with 51 (36.4%; 95% CI, 28.0%, 44.0%) showing significant level of pain reduction at the end of the trials, which represents an effect falling within the average normal range for placebo responses.

Withdrawal from the studies:

Only Deyo's 1990 study gave details of withdrawals (14%, 5 from each of the TENS and sham TENS groups) and their manage-

ment. They presented "a best-case analysis with assumptions that heavily favoured TENS therapy over sham-TENS therapy", with the assumption that every drop out from true TENS has a 25% improvement in each outcome at the four week follow-up, and that every drop out from sham TENS had scores unchanged from the baseline. In this analysis, the effect of TENS remained non-significant for every outcome except straight leg raising. There were no details of withdrawals from all the other studies.

At follow up:

There was no follow up in the Melzack 1983 or the Gemignani 1991 study. There was a two month follow up by Deyo 1990 where scores were reported to be nearly back to baseline. An unspecified time follow up by Jeans 1979 showed a gradual and continuing decrease in pain. A three and six months follow up by Thorsteinsson showed continuing pain relief. A three and six month follow up by Marchand showed that TENS and placebo still had positive effects on pain ratings but there were no significant differences between the two in comparison with the initial positive effects described in this trial. (See 'table of included studies' for further details).

Test for heterogeneity:

In order to check if the differences among the results of the trials were greater than could be expected by chance, an examination of the graphical displays of the results showed that the confidence intervals for the results of the studies all overlapped.

Test for homogeneity:

The Cochrane 'RevMan' software automatically tested for homogeneity of the results of the individual trials combined for each comparison in the review.

Sensitivity analysis (also see Appendix B (iv) for Metaview charts):

Testing the sensitivity of the results of the analysis to changes in the way it was done:

- (a) There were no changes in the inclusion/exclusion criteria.
- (b) No unpublished studies were identified following communication with leading researchers.
- (c) Excluded studies of lower methodological quality were included in the non-controlled studies review.

The sensitivity analysis supported the robustness of the review in relation to the key decisions and assumptions that were made in the process of conducting the review.

Publication bias:

There was an insufficient number of placebo controlled RCTS meeting the inclusion criteria (6) to consider using a 'funnel graph' to test the potential impact of publication bias on the results of this systematic review.

Summary of Analyses:

See Metaview figures below for graphical details bearing in mind that the pooling of data shown in the graphs represent the initial responses to treatment only rather than long term effects i.e. Deyo 1990 at 4 weeks, Thorsteinsson at 3 days, Melzack 1983 at 5 weeks, Marchand 1993 at 10 weeks, Gemignani 1991 at 3 weeks and Jeans 1979 at 4 days. It is also important to bear in mind that the studies of Gemignani and Jeans respectively included only ten subjects per group and ten overall, making their findings somewhat soft in relation to the conclusions suggested by this review. Due to the lack of suitable data in these trials, it was not possible to conduct a meta-analysis on long term effects, which would have been most desirable in view of the chronic low back pain subjects under study. Nevertheless the data represents the best available evidence from

TENS/ALTENS vs. placebo controlled trials we have to work with at the time of publication.

Discussion

This systematic review and meta-analysis, represents probably the best available evidence on the subject at this time and suggests one way forward in respect of confirming the efficacy of TENS/ALTENS in chronic low back pain with a powerful definitive trial for the future. However, this review was limited by the lack of good quality randomised controlled trials, only six studies out of seventy papers were identified as suitable for inclusion (as placebo controlled trials) and these six studies presented multipathology low back pain subjects, used different trial methodologies and varied in quality and strength as discussed in the text.

For example, the study by Marchand 1992 has been criticised for not being "truly randomised" i.e. a pseudo-randomisation with some matching of subjects and symptoms was described, however, this study was included in this review in view of its strengths and quality index as described in the text and we can see no valid reasons to exclude it. The reader may also be interested in the following recent critiques on Marchand 1993, see Robinson 1996 and Walsh 1997. Moreover, a sensitivity testing on the results of the meta-analysis was carried out by removing the Marchand 1993 study in order to assess the influence of this study on the meta-analysis and the results were as follows: The original meta-analysis for comparison 1. (TENS vs. placebo) gave an OR of 1.52(95%CI, 0.90,2.58) and for Comparison 3. (TENS/ALTENS vs. placebo) an OR of 2.11 (95%CI, 1.32,3.38). A new meta-analysis which excluded Marchand 1993 for comparison 1, (TENS vs. placebo) gave an OR of 1.39(95%CI, 0.80,2.46) and for Comparison 3, (TENS/ALTENS vs. placebo) an OR of 2.03(95%CI, 1.25,3.32). These results indicate that the inclusion of the Marchand 1993 study in this review did not significantly affect the results of the

original meta-analysis when an exclusion of this study was made during sensitivity testing.

Criticisms of Deyo's study by the reviewers and others (see Robinson 1996 and Walsh 1997) have prompted this reply from the original author via the comments and criticisms editor of the Cochrane Back Subgroup. "The Deyo study is a 2x2 factorial design, which seems widely misunderstood. The trial tested two independent treatments (TENS vs. Sham TENS, Exercise vs. no Exercise) in the same group of patients. In such a design, if there is no statistical interaction between the effects of the two treatments (exercise and TENS), then one is justified in combining the 2 TENS groups (with and without exercise) and the 2 sham TENS groups (with and without exercise) and one will obtain an unbiased estimate of the effect of TENS vs. sham TENS. This comparison will be more powerful, because of twice the sample size, than the uncombined groups. The study has been criticised by TENS advocates who do not understand the statistical advantages of the factorial design, and the fact that combining groups is not merely okay, but is desirable when there is no treatment interaction effect". The authors acknowledge these comments, however, this was in fact the primary analysis presented in the original review and its table of results and therefore does not affect the findings of the meta-analysis or the comments and criticisms of this study outlined in the Table of Characteristics of included studies.

In respect of the follow-up in the six studies, these were rather diverse and mostly for a short time and criticisms are justified. For example, the long term follow up by Deyo 1990 at three months and of Marchand 1993 at three and six months showed a near return to baseline conditions. There is therefore, little evidence to support the long-term effects of TENS/ALTENS in the treatment of chronic low back pain in the studies assessed. Further studies need to be done, mostly because of the lack of availability of proper studies in this field, which also reflects the lack of suitable follow-up studies at three and

six month intervals, and this is reflected in the recommendations section of this Cochrane Review.

One point of methodology has been raised, and the subject of some criticism, as we originally opted for not blinding the studies under review but recent guidelines taken from the Cochrane Handbook (1997) now recommend that "Reviewers must also decide whether those assessing study validity will be blinded to the names of the authors, institutions, journal and results of a trial when they apply critical appraisal criteria to the methods". Some empirical evidence suggests that blind assessment of reports might produce lower and more consistent scores than open assessments. However, such assessments are very time consuming. Reviewers must weigh the potential benefits of blind assessments against the costs involved in deciding whether or not to blind the reviewers". A recent study confirms this approach to be sound (Berlin 1997) and the results of their randomized trial demonstrated that blinding during study selection and data extraction had neither a clinically nor a statistically significant effect on the summary odds ratio, for the sample of five meta-analyses under study. Concluding that blinding is not necessary when conducting meta-analysis of randomised clinical trials.

The outcome of this systematic review provides some evidence to support the use of TENS and ALTENS in the management of chronic low back pain in comparison with the recent Canadian and Dutch studies which concluded that there was no evidence to support the efficacy of TENS in treating low back pain. The present study examined more than 100 studies to find the 70, which were subjected to the review process, to arrive at the final six included studies. Other reviews examined considerable fewer papers e.g. the Canadian study based their findings on only five RCT's (two of which were excluded from this review), two uncontrolled trials and three descriptive/expert opinion studies and the Dutch review only examined three trials (one of which was excluded from this review).

In conclusion, the outcome of this systematic review and meta-analysis confirms the beneficial therapeutic trend which may be expected from TENS and ALTENS therapies and provides some support for the current clinical practice of TENS and ALTENS in the treatment of chronic low back pain as follows:

- i. There is evidence to support the treatment of chronic back pain, at least in the short term, with TENS being more effective than placebo, but the evidence does not quite reach statistical significance unless pooled as a cumulative meta-analysis. There is no available evidence at this time to support the use of TENS treatment, as being more effective than placebo, in improving the range of motion in patients with chronic back pain.
- ii. There is evidence, which is statistically significant, to support the treatment of chronic back pain with acupuncture-like ALTENS for pain relief, at least in the short term, being more effective than placebo. There is also evidence that ALTENS treatment improves the range of motion of subjects with chronic back pain, being more effective than placebo, at least in the short term.
- iii. There is statistically significant evidence from pooling the TENS and ALTENS data in a cumulative meta-analysis to indicate that the use of TENS/ALTENS for the treatment of chronic back pain, at least in the short term, could have been shown to be beneficial almost 20 years ago.
- iv. There is no data available to support the notion that TENS or ALTENS is successful in returning patients to work faster than alternative treatments.
- v. There is no difference on functional outcomes between TENS/ALTENS and Placebo
- vi. The use of TENS/ALTENS is relatively free from side effects in comparison with a credible placebo treatment.

The authors of this review accept that the available evidence published in the English language remains rather weak, even after twenty-five years or more of research and publishing. This updated

review, at January 1998, actively sought to review publications of trials in non-English languages for inclusion. So far, we have been unable to identify any non-English language publications of placebo controlled RCTS of TENS/ALTENS for the treatment of chronic low back pain. However, if readers of this review can help us in this task then please contact us via E-mail (contact address at the end of this review).

Albeit at this stage in our knowledge, and until we can find, access, and review these elusive non-English language studies, the only way the question of the efficacy of conventional and acupuncture-like transcutaneous electrical nerve stimulation in the treatment of chronic low back pain can be answered definitively is to conduct a new, well designed and powerful, double-blind, randomised (with adequate allocation concealment) placebo controlled trial as discussed in the next section of this review.

Implications for practice

Generalisability

The subjects of the studies that make up this review were not only from several types of care cultures, but also involved both sexes, with a wide range of ages, with multipathology chronic low-back pain. Many subjects had had previous unsuccessful surgery. There were some dissimilarities between the trials from Europe, Canada and the USA, but the overall methodology was comparable in terms of this review.

Cost/Benefit Balance

Transcutaneous electrical nerve stimulation as TENS or ALTENS appears to be a suitable, inexpensive, therapeutic technique, more effective than placebo for relieving pain and improving the range of movement in chronic low back pain patients. The procedure should be considered for inclusion in the treatment programme of these patients including those with failed lumbar surgery. There is little evi-

dence of harmful side effects from these treatments apart from mild skin reactions and occasional temporary worsening of the perception of pain.

Whilst the techniques of TENS and ALTENS cannot be regarded as a panacea for the treatment of multipathology chronic low back pain, it is suggested by this review that these techniques have a role to play in the rehabilitation of these patients, as part of an overall treatment programme. This programme might include, exercise regimes, other physical treatments including hot and cold applications, medication, surgery and psychological techniques. Self-administered treatment at home with a suitable unit would also be worthy of consideration as a cost-effective therapeutic strategy.

Implications for research

A definitive research study is needed to strengthen and consolidate the last twenty-five years of TENS and ALTENS research. This should take the form of a well designed, double-blind randomised placebo controlled trial, which takes into account the following parameters:

1. a three or four arm study which compares (a) TENS, (b) ALTENS with (c) a credible placebo and/or (d) a no treatment control.
2. a study with at least 80% power of detecting a difference of clinical importance on the chosen measurement scales, using statistical methods of power calculations to determine the required number of patients to meet the trial outcomes based on the results of the meta-analysis of the studies in this review, ideally as a multi-centre study with adequate blinding of subjects, therapists and assessors.
3. with adequate allocation concealment and a quality-based trial structure (after Chalmers 1981).
4. with the construction of a standardised intervention with adequate baseline matching of subjects and preferably using a suitable, specific, differential diagnostic procedure for low-back pain e.g. Sweetman (1992).

5. with set electrical parameters for TENS and ALTENS, electrode placements, length of treatments, outcome measurements for pain, range of movement/activity, functional status and return to work, with adequate follow-up at three and six month intervals.

6. and by eliminating as far as possible all other treatment variables with the exception, perhaps, of a set of simple flexion and extension lumbar exercises for all subjects which would be in keeping with the current practice of remedial exercises for low back pain

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Conflict of interest:

Gordon Gadsby is a clinical advisor to Body Clock Health Care Ltd and organising officer of The Society of Electrotherapists; Dr Michael Flowerdew is an executive member of The Society of Electrotherapists.

4.5.3 Conclusions

This section presented the complete Cochrane Review in its extracted version from the RevMan software prior to submission and inclusion in the next edition of the Cochrane Library Issue 2 (1998). For traditionally published research papers in professional journals this would be its final format, subject perhaps to further research and republication of updated papers. There is, therefore, little opportunity in traditional publishing for responding to comments and criticisms satisfactorily, apart from letters to the editor and updating articles following new research.

However, one of the exciting mechanisms now available to authors of Cochrane Reviews using electronic media, is the opportunity to continually improve and update their reviews through the Comments and Criticisms section of the Cochrane Library (also see the latest edition of the Cochrane Library on CD-ROM for the latest update). This is in addition to the ongoing inclusion of newly published studies, meeting the inclusion criteria for this review, and responding to comments and criticisms from other sources such as editorial comments and invited commentaries in evidence-based medicine and allied journals.

The next section (4.6), following the tables and charts extracted in RevMan format as referenced above, will examine in some detail the Cochrane Collaboration comments and criticisms mechanisms, which are aimed at improving and updating Cochrane Reviews, and to discuss their application to the Cochrane Review under consideration in this thesis, in order to show how and why improvements may be necessary in order to improve the quality and content of an ongoing review.

Figures XXIII: XXIV: XXV:

Tables and Charts extracted from the Cochrane Library and Metaview Software:

Figure XXIII: Characteristics of included studies table

Figure XXIV: Characteristics of excluded studies table

Figure XXV: Metaview Charts

1. Summary Chart of the 7 comparisons of TENS/ALTENS
2. Comparison 1. TENS vs. Placebo in pain reduction
3. Comparison 2. ALTENS vs. Placebo in pain reduction
4. Comparison 3. TENS/ALTENS vs. Placebo in pain reduction
5. Comparison 5. ALTENS vs. Placebo and change in ROM
6. Comparison 10. TENS/ALTENS vs. Placebo - treatment side effects.
7. Cumulative meta-analysis of Comparison 1.
TENS vs. Placebo in pain reduction
8. Cumulative meta-analysis of Comparison 3.
TENS/ALTENS vs. Placebo in pain reduction

The effectiveness of transcutaneous electrical nerve stimulation and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain

Study	Method	Participants	Interventions	Outcomes	Notes
Deyo/Walsh 1990	A RCT of TENS and/or ALTENS as modulated waveforms - not a standardised intervention, a partial allocation concealment by sealed envelopes and random numbers, not described as double-blind - blind to subject, subjects recruited by advert/ heavily screened before trial, outcome measured by VAS and ROM/SLR.	145 subjects (120 after dropouts) from San Antonio, USA, as a self-referred source population, including 42 post-surgery or chymopapain therapy subjects with 19 allocated to the TENS group alone (61%); in the ratios of (19:3:10:10); Average age 51.4 years, median length of pain 4.1 years.	4 groups as TENS and/or ALTENS, Sham TENS, TENS with exercise and Sham TENS with exercise; with electrode placement initially over the area of pain and then moved to optimise pain control; 1. TENS (n=31) @ 80-100 or 2-4Hz x 45 minutes x 42 treatments; 2. TENS + exercise (n=34); 3. Sham TENS ((n=31) and no exercise; 4. Sham TENS (n=29) + exercise. N.B. all groups also had hot packs/pads - a mean of 23 days x 45mins.	Appropriate and valid outcome measures for pain and activity, showed improvement in all groups but no clinically or statistically significant treatment differences between the four. At 2 months follow-up scores nearly back to baseline; one third reported minor side-effects as skin irritations, data and statistical presentations satisfactory, but too many groups and variables for satisfactory model validity. Initial outcome at 4 weeks: no. of patients improved not given, results given as VAS pain score changes: TENS = 47%; SHAM TENS = 42%.	A good sample size trial with participants meeting the inclusion criteria, internal and external validity satisfactory but too many variables e.g. 23% TENS 77% ALTENS, variable electrode placements, plus additional hot packs/ heating pads etc. and uneven post-surgery matching. A high withdrawal rate above 14% in the first 3 months and over 16% in the following months though this was handled satisfactorily at the analysis stage. Quality Index = 0.84
Gemignani 1991	A double-blind RCT of ALTENS as a standardised intervention, with allocation concealment using a table of random numbers and the paired/unpaired method, not clear how 'blind' patients were, outcomes measured by VAS and ROM test - Schober's test, baseline matching satisfactory, used a credible placebo.	20 subjects (10 per group) from the University of Pisa, Italy, 10M/10F, Age 24-59, all diagnosed with chronic lumbar pain and stiffness of at least 1 month's duration (2-60 months) in ankylosing spondylitis subjects - no previous surgery indicated.	ALTENS at 5Hz (n=10) and a credible sham placebo control (n=10), with electrode placements to low-back acupuncture points x 20 minutes x 10 treatments.	A significant or trend difference in favour of ALTENS regarding pain, less obvious in stiffness, appropriate pain and activity measurements, assessed by a blinded evaluator, no side-effects recorded, no follow-up, data and statistical presentations satisfactory, model validity satisfactory. Initial outcome at 3 weeks: % improved as ALTENS = 90%; PLACEBO = 40%; Difference = 50%.	A pilot study with low power, with good response to real treatments, satisfactory response to placebo, no further studies carried out. No withdrawals from the trial recorded. Quality Index = 0.55

The effectiveness of transcutaneous electrical nerve stimulation and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain

Jeans 1979	A double blind RCT with no details of allocation concealment, randomisation method or inclusion exclusion criteria, outcomes measured by McGill Pain Questionnaire, small sample size - low power.	6 low-back pain subjects, M/F not known, Age 33-76years - mean = 47.4, 16 subjects in trial including 6 LBP - no further details of source population.	TENS at 60Hz as a standardised intervention with electrode placement over local pain, distal trigger or acupuncture points, sham at site of pain and distant, non-relevant points x 2/day x 4 days i.e. 1. TENS (n=6) @ 60Hz x 8 treatments - no details of length of treatments, 2. control = dead machine (n=4) 4 modes of application as above.	Appropriate and valid outcome measures for pain which showed a 40% reduction in pain scores with TENS at local pain area points and 10% at other points, no side-effects reported, follow-up of LBP subjects showed gradual decreases in pain intensity and radiating pain over a period of a few weeks, data and statistical presentations satisfactory, model validity satisfactory. Initial outcome at 4 days: % change in scores TENS = 40%; CONTROL = 10%; Difference = 30%	An acceptable pilot trial but with very low numbers for LBP (6) and many variables i.e. 4 treatment conditions with 16 subjects and difficult to extract the relevant data. No withdrawals from the trial recorded. Quality Index = 0.55
Marchand 1993	A RCT with a partial allocation concealment - not described as double-blind but? single-blind, patients recruited by medical referral and local advertising with clinical exclusion criteria after Nachemson (1980), all treatment groups had good baseline matching, no details of previous surgery. Outcome measured by VAS scores for pain intensity and unpleasantness.	42 subjects; 20M/22F; Average age 36 years; Source - University of Quebec Pain Lab, Canada, average length of pain 9 years, adequate source population including ankylosing spondylitis patients etc, mainly as self-referrals to the trial.	1. TENS (n=14) at 100Hz as a standardised intervention x 30 minutes x 20 treatments. 2. a credible placebo TENS (n=12), 3. no treatment control group(n=14), with electrode placement appropriate to the dermatome involved.	Appropriate and valid outcome measures for pain and unpleasantness, using separate visual analog scales to measure sensory-discriminative and motivational-affective components of low-back pain, and which showed TENS to be significantly more effective than placebo TENS for pain at 1 week, but not at long-term follow-up and not more effective than placebo in reducing unpleasantness - but the starting values were lower in TENS group. No side-effects shown, no activity data given, data and statistical presentations satisfactory. Initial outcome at 10 weeks: No of patients improved not given; Results given as score changes i.e. reduction in VAS pain scores: TENS = 43%, Placebo = 18%, Difference = 25%	An acceptable pilot study size trial with satisfactory internal, external and model validity. No withdrawals from the trial recorded. Some evidence to support the cumulative effect of conventional TENS also described. Quality Index = 0.57

The effectiveness of transcutaneous electrical nerve stimulation and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain

Melzack/Vetere 1983	A double-blind RCT of ALTENS, as a standardised intervention, and with an adequate allocation concealment using the sealed envelope method, researcher selected suitable candidates from referrals to physiotherapy dept, outcomes measured by McGill Pain Questionnaire (MPQ) and two Range Of Motion (ROM) tests for activity. In addition, all participants had standard exercises for low back pain after each treatment.	41 subjects, 19M/22F, average age 46.3 years, from a Physiotherapy Dept Canada, average length of pain 36.2 weeks, subjects ambulant and intelligent, adequate source population with no details of previous surgery.	1. ALTENS (n=20) at 4-8Hz with electrode placement over the pain site and one on the lateral aspect of the thigh x 30 minutes x up to 10 treatments, average of 5.1 treatments, over a two-week period. 2. gentle mechanical massage using four skin pressure suction cups administered by a physical therapist as the control (n=21). 3. no placebo control group.	Appropriate and valid outcome measures for pain and activity, which showed TENS to be more effective than mechanical massage for pain relief, and also gave an increased range of movement, no side-effects, no follow up data, statistical presentations satisfactory. Initial outcome at 5 weeks: % improved on ALTENS = 85%, Control = 38%, Difference = 47%	An acceptable trial with participants meeting the inclusion criteria, adequate internal, external and model validity. ? effect of standard exercises on the outcomes. No withdrawals from the trial recorded. Quality Index = 0.70
Thorsteinsson	A cross-over RCT of TENS - 3 real treatments and 3 placebo over 3 days, adequate allocation concealment randomised by medical statistics department, a double-blind trial with no washout period, a non-standardised intervention, adequate baseline matching with 30 post-surgery cases, outcomes measured by NRS (Numerical Rating Scale) 4 point scale (-1 to +2) for pain plus personality assessments (Minnesota Multiphasic Personality Inventory).	33 LBP subjects, from the Dept of Phys Med Mayo USA, 11M/22F, average age 48.6 years, 30 had had previous surgery (1-10 operations), adequate source population mainly of post-surgery cases and some with arthritis.	1. TENS at 15-180Hz (n=33) 2. cross-over placebo, with output/frequencies adjusted for each patient, x 20 minutes, x 3 treatments, with electrode placement applied over 3 predetermined sites.	Valid outcome measurement techniques, side-effects as allergic reactions and aggravation of pain n=5, data and statistical presentations satisfactory. Initial outcome at 3 days: % improved on TENS = 48.7%; CONTROL = 32.3%; Difference 16.4%. Follow-up of 48 subjects on home care, by questionnaire, at 3 months and 6 months with 56.25% and 43.75% respectively still using the modality.	Low model validity - too many variables, with the best results from TENS when applied over the site of the low-back pain, rather than over a related nerve trunk or unrelated nerve trunk. No withdrawals from the trial recorded. Quality Index = 0.71

Characteristics of Excluded Studies

Study Identifier	Reason for exclusion
Abram 1983	An uncontrolled, cross-over trial of electroacupuncture (EAP), placebo electro-acupuncture (at non-acupuncture sites) and ALTENS with no allocation concealment or blinding (though sessions were randomly arranged), no baseline matching, group comparability or placebo control group. VAS scoring method for pain assessment both before and 48 hours after treatment but no activity outcome assessments.
Andersonn 1976	An uncontrolled cross-over trial of TENS/ALTENS, not as standardized interventions and with different numbers of treatment; no randomisation, blinding or placebo control group; no baseline matching or comparability of source population, no wash-out period; VRS measurement method for pain but no valid activity assessment.
Barr 1987	An uncontrolled trial of Sham TENS vs. continuous TENS vs. pulsed TENS with chronic pain subjects of mixed etiology. Few details of trial methodology and statistical data given with subjects not described as chronic low back pain.
Bates 1980	An uncontrolled trial of TENS in a self-selected group of 36 LBP subjects out of a 235 mixed pathology group. Insufficient data on the low back pain patients to know how they responded to treatment and only 29 patients carried on the treatment for more than one week.
Brill 1985	An uncontrolled study of TENS, not a standardized intervention with no randomisation, baseline matching or blinding described; a subjective evaluation of pain by patient using a % method, and an activity assessment as to whether or not back at work after 12 months.
Cassuto 1993	An uncontrolled trial of high frequency TENS on self-selected patients with mixed pathologies, no randomisation or blinding described, VAS scale for pain assessment before and after daily treatment, no activity assessment described.
Cheng 1987	An uncontrolled trial to compare ALTENS vs. (EAP) for chronic back pain using a novel approach called the 'Codetron' unit with adequate baseline matching and group comparability, trial described as randomised but no details given.
Chilton 1993	A report on only 3 case studies therefore excluded from the review.
Coletta 1988	An uncontrolled trial of TENS vs. TENS and local etofenamate ointment, not a standardised intervention, described as a RCT but no placebo control, no details of randomisation, baseline matching or blinding techniques described, no inclusion/exclusion criteria, NRS for pain measurement.

Characteristics of Excluded Studies

Coli 1992	An uncontrolled trial of TENS vs. an association group of galvanic + dyadinamic + TENS with no placebo control group. No details of randomisation or blinding given. This study did not meet the inclusion criteria for a randomised controlled trial comparing an active TENS/ALTENS treatment with a placebo treatment.
Davis 1975	An uncontrolled study of TENS with no details of randomisation, blinding or assessment measures given and no details of baseline matching or inclusion/exclusion criteria.
Denning 1988	A retrospective report by questionnaire of TENS usage in 182 patients of which 100 replies were used, no randomisation or blinding, no baseline matching or group comparability, VAS pain measurement.
Eriksson 1979	An uncontrolled study of TENS and ALTENS, no standardisation of intervention, no details of blinding, randomisation, baseline matching or inclusion/ exclusion criteria, VAS assessment for pain.
Ersek 1976	An uncontrolled study of ALTENS using 35 consecutive patients of which 13 had low back pain - no details of randomisation, blinding or baseline matching, no credible outcome assessment measures other than a % rating for pain relief, no activity assessments.
Fargas-Bajak 1992	An uncontrolled trial of ALTENS using the novel Codetron unit and using self-selected subjects with chronic low back pain over a two year period, also with the use of home care units No details of blinding etc, pain outcomes measured by a modified VAS, no activity assessments.
Field 1991	A double-blind controlled trial of TENS and Burst TENS but with few details of trial methodology and no suitable outcome data. No reply to a request for further trial information therefore excluded from the review.
Fox 1976	An uncontrolled cross-over, non-RCT trial of TENS vs. acupuncture as a standardised intervention, no randomisation, blinding, baseline matching, inclusion/exclusion criteria or washout period described, outcome assessment of pain with McGill pain questionnaire as PPI and PRI. This study did not meet the inclusion criteria for a randomised controlled trial comparing an active TENS/ALTENS treatment with a placebo treatment.
Fried 1984	A retrospective review of TENS - no standardisation of intervention no randomisation, baseline matching, blinding, inclusion/ exclusion criteria or outcome assessment descriptions - a set of observations.
Gunn 1975	A retrospective review of 100 low back pain subjects treated with TENS, no standardisation of intervention, baseline matching, randomisation or blinding but therapists counselled against bias, no validated pain/activity outcome assessment measures.

Characteristics of Excluded Studies

Hery 1987	An uncontrolled trial of TENS vs. epidural but few details of trial methodology given. A significant relief of pain obtained with TENS but few statistics presented.
Hsieh 1992	A randomised trial of TENS as Transcutaneous Muscular Stimulation using a four way comparison with chiropractic, massage and corset. This study excluded from the review due to lack of suitable placebo control and outcome statistics.
Indeck 1975	An uncontrolled study of TENS but no details of experimental design, randomisation, blinding, baseline matching, or standardisation of intervention given, VAS assessment for pain, no details of activity assessments.
Jarzem 1997	<p>Abstract available on: http://www.aaos.org/wordhtml/anmeet97/sciprog/315 as: "The authors examined the effectiveness of three types of Transcutaneous Electrical Nerve Stimulation (TENS) for the treatment of chronic low back pain (LBP). Three hundred twenty-four patients with LBP, mean duration 6 years were randomly allocated to receive 4 weeks of treatment with conventional TENS (n = 84), Nu-waveform TENS (n = 79), and sham TENS (n = 83). Outcome measures included functional scales, physical measures, and the zung depression scale. At the end of treatment, no statistically significant treatment effects were noted in any of the nine outcome measures, $F(27,942) = 0.78$, $p < 0.78$. There was a significant omnibus time effect, $F(18,303) = 8.42$, $p < .0001$. There were no significant effects of TENS with time, $F(54,915) = 1.24$, $p < 0.12$. The authors conclude that for patients with chronic LBP, a 4-week course of TENS treatment is no more effective than treatment with a placebo".</p> <p>Reasons for exclusion: The authors of this review are unable to include the above study in the meta-analysis until we obtain the following information, which is not recorded in the conference paper. A request has been made for this information which is now awaited from the study's main author.</p> <ol style="list-style-type: none">1. Details of the allocation/randomisation procedure2. Details of the electrical parameters used in the study including waveform, frequencies, pulse widths, site of electrode application, recommended length of each treatment, number of treatment/day/week/trial.3. Basic technical details of the Nu-waveform mode.4. Results: the numbers of patients improved/not improved, especially in relation to pain control and range of motion, for each of the four treatments at 4 weeks and 3 months and/or number of patients with significant/ not significant changes ($>20\%$?), from the baseline readings, in order to obtain data in a form which is compatible with the other study outcomes and in order to enter this data into the meta-analysis.5. Information on long-term effects at 6 months and 1 year if

Characteristics of Excluded Studies

Jarzem 1997 cont.	<p>available.</p> <p>6. Were the trial numbers estimated a priori?</p> <p>7. Was the adequacy of randomisation and blinding evaluated by questionnaire post trial?</p> <p>8. Details of the exercise regime followed by all groups?</p> <p>Were additional therapeutic interventions applied e.g. hot packs or pads (as in Deyo 1990) or cold packs etc?</p> <p>It is necessary to obtain this information before proceeding further insofar as this data is unpublished material, which has not yet been subjected to the peer review process. However, there are critics of the peer-review process insofar as most journals do not have explicit criteria for manuscript review and rely on the expert judgement of expert reviewers. This leaves the process open to arbitrariness and to systematic bias in contrast with the assessment of methodological quality that is an integral part of a rigorous Cochrane review.</p> <p>However, it is generally felt "that while inclusion of unpublished data in scientific overviews remains controversial, most investigators directly involved in meta-analysis believe that unpublished data should not be systematically excluded. The most valid synthesis of available information will result when meta-analysts subject published and unpublished material to the same rigorous methodological evaluation and present results with and without unpublished sources of data" (Cook 1993).</p> <p>The authors hope to review this study, in due course, in the light of these recommendations and within the framework of the Cochrane Collaboration. It is also intended to conduct a sensitivity analysis in which the results will be presented both with and without any unpublished studies in order to demonstrate whether both analyses point to the same conclusion i.e. that the inferences are relatively strong. If inclusion of any unpublished studies substantially diminishes the magnitude of treatment effect, any inferences made on the basis of this analysis will be much weaker (Cook 1993).</p>
Johansson 1980	An uncontrolled trial of TENS with an unidentified number of chronic low back pain subjects. A 50% overall improvement in pain relief but no details of the low back pain subgroup.
Johnson 1992	A retrospective study of long-term TENS for pain relief over a ten year period. This study did not meet the inclusion criteria.
Johnson 1993	A prospective study of responses to TENS at various frequencies and modes including 4 subjects with low back pain. This study excluded from this review because of the large number of experimental variables and too few relevant subjects.
Laitinen 1976	An uncontrolled, non-RCT, comparative trial between acupuncture and TENS, no randomisation, blinding or inclusion/ exclusion criteria described, VRS pain assessments by doctor and by the patient. This study did not meet the inclusion criteria for a randomised controlled trial comparing an active TENS/ALTENS treatment with a placebo treatment.

Characteristics of Excluded Studies

Lampe 1987	A 5-day cross-over study of TENS for back pain, no details of randomisation or blinding, an adequate source population and sample size, VAS scale for pain. This study did not meet the inclusion criteria.
Ledergerber 1979	An uncontrolled trial of a novel ALTENS system vs. conventional TENS, no randomisation, blinding, baseline matching or outcome measures described, the novel ALTENS used for moderate pain and conventional TENS for severe pain.
Lehmann 1983	A trial of subthreshold continuous TENS, EAP and a placebo group but with few experimental details given. No suitable outcome statistics available from the data.
Lerner/Kirsh 1981	A double-blind retrospective case-control comparative study of ALTENS (n=20) and placebo but with few details of allocation concealment, randomisation, blinding or baseline matching, pain outcome measured by daily 2 hourly pain charts.
Linzer 1976	An uncontrolled trial of variable TENS, patient determined electrical stimulation parameters and electrode locations with 10 low back pain subjects from a larger multipathology study of 100. Few details of trial methodology, of outcome measures used and data.
Loeser 1975	An uncontrolled trial of TENS with no standardisation of the treatment intervention, randomisation, blinding, no description of outcome measures used, no inclusion/ exclusion criteria or details of baseline matching or group comparability.
Long 1974	An uncontrolled study of TENS with no standardisation of intervention, no randomisation, blinding or validated pain/activity outcome measures described, no details of baseline matching or previous surgery.
Long 1979	An uncontrolled study of TENS following on from Long (1974), no details of electrode placements, electrical parameters, no standardisation of intervention, no randomisation or blinding techniques described, no inclusion/ exclusion criteria, pain intensity measured on a NRS scale of 0-4.
Lundeberg 1984	A trial of TENS and ALTENS with subjects randomised to 1 of 6 groups, not a standardised intervention - too many variables, no blinding, no details of baseline matching, previous surgery or inclusion/ exclusion criteria described, outcome assessment by McGill Pain Questionnaire and VAS scales.
Macdonald 1983	This was a placebo controlled trial of superficial acupuncture (4mm depth) vs. placebo for chronic low back pain and was not a trial of TENS or ALTENS vs. placebo.

Characteristics of Excluded Studies

Magbagbeola 1987	An uncontrolled trial of TENS and ALTENS, with the use of analgesics discouraged during the trial, not a standardised intervention, no randomisation, no inclusion/exclusion criteria, blinding, no details of baseline matching or group comparability, and pain/activity outcome measures not described.
McDonnell 1980	An uncontrolled trial of conventional TENS with no details of standardisation of the intervention, randomisation, blinding, baseline matching, inclusion/exclusion criteria or outcome measures used.
Melzack 1975	An uncontrolled trial of TENS and ALTENS, not as a standardised intervention, no randomisation, blinding, baseline matching or inclusion/exclusion criteria described, NRS and McGill Pain Questionnaire for outcome measurements.
Melzack 1980	A cross-over, non-RCT, design trial of continuous ALTENS as a standardised intervention vs. ice massage, no blinding, no baseline matching, group comparability, no inclusion/exclusion criteria or concealed randomisation described, McGill Pain Questionnaire assessment of pain, no activity assessments described. This study did not meet the inclusion criteria for a randomised controlled trial comparing an active TENS/ALTENS treatment with a placebo treatment.
Meyler 1994	An uncontrolled trial of TENS, no standardisation of the intervention - patients controlled the electrical parameters, no details of randomisation, blinding, baseline matching, previous surgery or inclusion/exclusion criteria described, % scoring for outcome measurements of pain intensity/alleviation plus physical examinations.
Moore & Shurman 1997	This was a preliminary and experimental study of 24 patients which compared neuromuscular electrical stimulation, transcutaneous electrical nerve stimulation, a combination of both of these treatment and a placebo, using a cross-over design in the treatment of multipathology chronic back pain subjects. The treatments were self administered, using a standardised intervention of 2 x 300 minutes each of the four treatments, with a 2-day wash out period between each treatment and used variable electrode placement. Inclusion and exclusion criteria were satisfactory and good pain outcome assessments were made but we were unable to extract suitable data for pooling in the meta-analysis. There were no indications that assessors were blinded and there was no follow up assessments. This experimental 14-day study used 4 different modes of treatment for each subject, does not reflect clinical utility, and was therefore not suitable for inclusion in this review.
Moore 1983	An uncontrolled trial of TENS and ALTENS as a standardised intervention, no details of selection, randomisation, blinding or details of inclusion/exclusion criteria, previous surgery or baseline matching, outcome measurements as a % of pain reduction.

Characteristics of Excluded Studies

Pontinen 1979	An uncontrolled trial of acupuncture vs. TENS which was not suitable for inclusion in this review because of a lack of methodological details and suitable data for the statistical evaluation of patient responses to TENS or acupuncture.
Pope 1994	A comparative trial of 4 treatment groups for low back pain as manipulation, a modulated burst transcutaneous muscular stimulation (TMS), massage and corset. Few details of trial methodology given and insufficient data to assess the numbers of subjects responding to the four treatments.
Procacci 1982	An uncontrolled trial of continuous TENS as a standardised intervention, no details of randomisation, matching, blinding, inclusion/exclusion criteria, or details of outcome measures apart from the clinical examination.
Richardson 1980	An uncontrolled trial of TENS, no details of trial methodology or baseline matching described, numerous but valid outcome measures used. (also see Richardson 1981)
Rutowski 1977	An uncontrolled trial of electrostimulation using needles as electrodes rather than surface electrodes so therefore this study was excluded from the review.
Schuster 1980	A comparative study of TENS and post-operative narcotic analgesia after low back pain surgery but no suitable outcome measures given.
Shealy 1974a	A retrospective study of 200 patients with chronic low back pain and/or sciatica treated with TENS, few details of trial methodology, baseline matching, previous surgery or outcome measures used.
Sodipo 1981	A cross-over trial of TENS, not as a standardised intervention, no details of randomisation, blinding, electrical parameters, baseline matching, inclusion/exclusion criteria or wash-out period, satisfactory outcome measures as PPI for pain but no activity assessments.
Thurin 1980	An uncontrolled study of TENS with no details of experimental design, baseline matching, pain or activity outcome measures.
Timm 1994	A randomised trial of a wide range of different treatments including TENS (which was included with hot packs and ultrasound). TENS treatment on its own was not assessed.
Tulgar 1991a	An uncontrolled comparative study of three different waveforms used in TENS, patients blind to waveform, electrode placement for optimal distribution of paraesthesia, no inclusion/exclusion criteria stated, no details of randomisation or baseline matching, VAS pain measurement but no activity assessments.

Characteristics of Excluded Studies

Tulgar 1991b	A comparative study of different waveforms used in TENS, double-blind only regarding the different active wave forms, no baseline matching, VAS scale for pain assessment, no activity assessments.
Van Doorn 1981	An uncontrolled trial of TENS with no details of the electrical parameters or outcome assessment measures.
Walmsley 1979	An uncontrolled trial of continuous variable TENS, no details of randomisation, baseline matching or blinding described, McGill Pain Questionnaire for outcome measurement.
Wolf 1981	An uncontrolled trial of continuous TENS with patient determined stimulation frequencies and with 30% of subjects having only one treatment. This study was excluded from the review because of the poor identification of low back pain subjects and the lack of suitable data.
Wynn Parry 1988	An uncontrolled prospective study of TENS (n = 101), as part of a rehabilitation programme using a variety of pain relief techniques, no details of a standardised intervention, blinding, randomisation, electrical parameters or electrode placements, no details of outcome measures used.

Figure XXV: Metaview Charts:**1. Summary Chart of the 7 comparisons of TENS/ALTENS**

Review: TENS/ALTENS effectiveness in chronic low back pain

Comparison or Outcome

Peto Odds Ratio
(95%CI)

TENS/ALTENS vs Placebo in chronic back pain

TENS vs Placebo in pain reduction - Comparis

ALTENS vs Placebo in pain reduction - Compa

(AL)TENS vs Placebo in pain reduction - Com

ALTENS vs Placebo - change in ROM - Comp

(AL)TENS vs Placebo and side effects - Comp

Cumulative meta-analysis-Comparison 1-sort b

Cumulative meta-analysis-Comparison 3-sort b

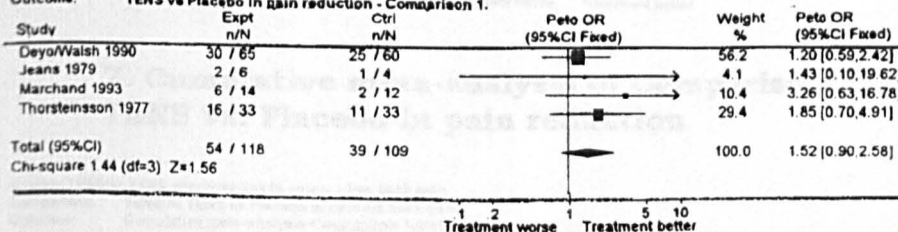
1 .2 1 5 10

2. Comparison 1. TENS vs. Placebo in pain reduction

Review: TENS/ALTENS effectiveness in chronic low back pain

Comparison: TENS/ALTENS vs Placebo in chronic back pain

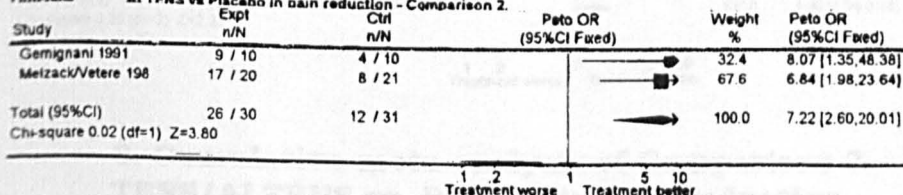
Outcome: TENS vs Placebo in pain reduction - Comparison 1.

**3. Comparison 2. ALTENS vs. Placebo in pain reduction**

Review: TENS/ALTENS effectiveness in chronic low back pain

Comparison: TENS/ALTENS vs Placebo in chronic back pain

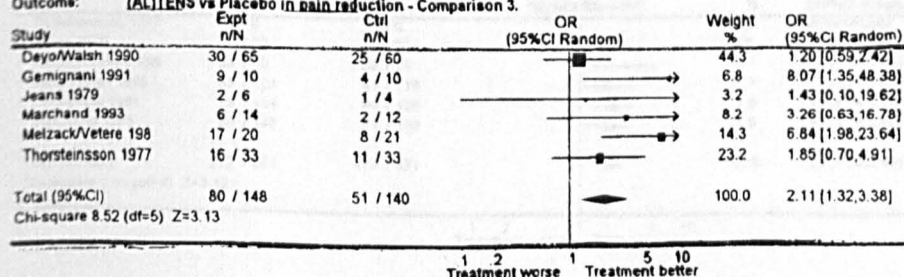
Outcome: ALTENS vs Placebo in pain reduction - Comparison 2.

**4. Comparison 3. TENS/ALTENS vs. Placebo in pain reduction**

Review: TENS/ALTENS effectiveness in chronic low back pain

Comparison: TENS/ALTENS vs Placebo in chronic back pain

Outcome: (AL)TENS vs Placebo in pain reduction - Comparison 3.

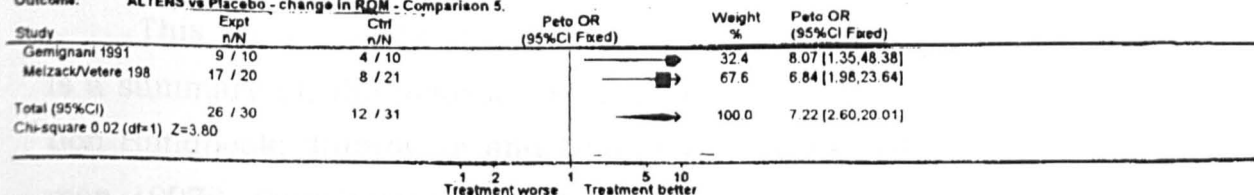


5. Comparison 5. ALTENS vs. Placebo and change in ROM

Review: TENS/ALTENS effectiveness in chronic low back pain

Comparison: TENS/ALTENS vs Placebo in chronic back pain

Outcome: ALTENS vs Placebo - change in ROM - Comparison 5.

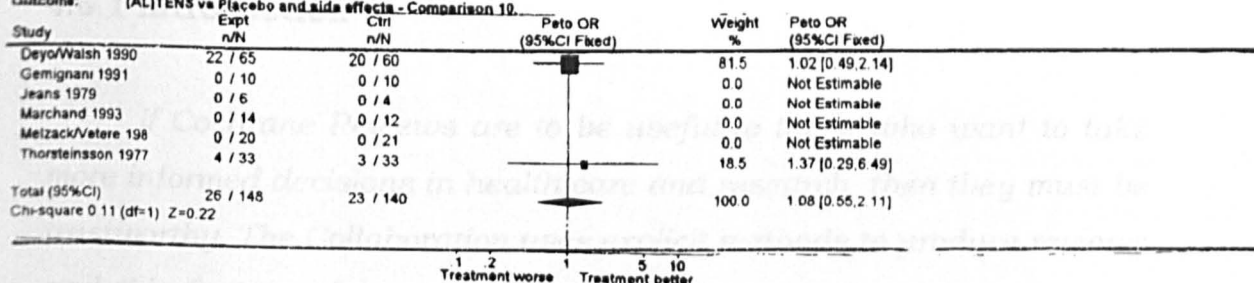


6. Comparison 10. TENS/ALTENS vs. Placebo - treatment side effects.

Review: TENS/ALTENS effectiveness in chronic low back pain

Comparison: TENS/ALTENS vs Placebo in chronic back pain

Outcome: (AL)TENS vs Placebo and side effects - Comparison 10.

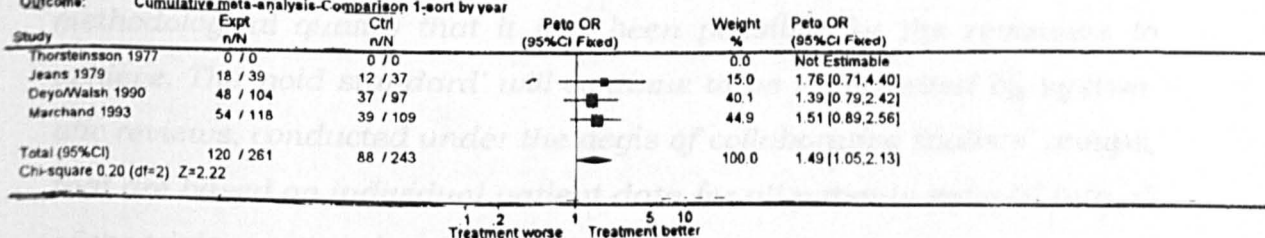


7. Cumulative meta-analysis of Comparison 1. TENS vs. Placebo in pain reduction

Review: TENS/ALTENS effectiveness in chronic low back pain

Comparison: TENS/ALTENS vs Placebo in chronic back pain

Outcome: Cumulative meta-analysis-Comparison 1-sort by year

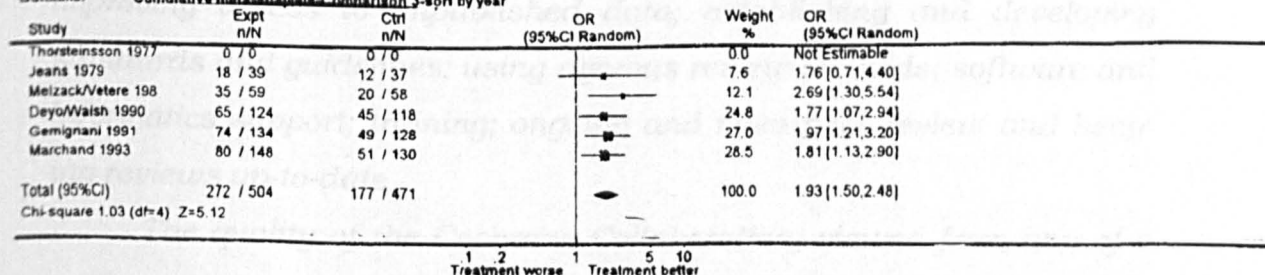


8. Cumulative meta-analysis of Comparison 3. TENS/ALTENS vs. Placebo in pain reduction

Review: TENS/ALTENS effectiveness in chronic low back pain

Comparison: TENS/ALTENS vs Placebo in chronic back pain

Outcome: Cumulative meta-analysis-Comparison 3-sort by year



4.6 Improving and Updating Reviews

This section of the thesis is structured on, extracted from, and is a summary of, the following section from the Cochrane Collaboration Handbook: 'Improving and Updating Reviews', (Mulrow and Oxman 1997j). Supplementary material, again using a case study approach, is in the form of an application commentary/action taken, outlining the authors' use of these guidelines in improving and updating the Cochrane Review under consideration in this thesis.

4.6.1 Introduction

If Cochrane Reviews are to be useful to those who want to take more informed decisions in health care and research, then they must be trustworthy. The Collaboration uses explicit methods to produce reviews and this feature alone will make them more useful to users than the vast majority of reviews that are currently available. Above a certain guaranteed minimum standard, the reviews contributed to The Cochrane Database of Systematic Reviews (CDSR) will vary in the level of methodological quality that it has been possible for the reviewers to achieve. The 'gold standard' will continue to be represented by systematic reviews, conducted under the aegis of collaborative trialists' groups, that are based on individual patient data for all patients entered into all of the trials meeting the entry criteria for the review.

Mechanisms for maintaining and raising the standards of Cochrane Reviews include: attracting dedicated participants and avoiding conflicts of interest; Consumer involvement; ensuring access to studies; improving access to unpublished data; establishing and developing standards and guidelines; using rigorous review methods; software and informatics support; training; ongoing and open peer review and keeping reviews up-to-date

The quality of the Cochrane Collaboration, viewed from any of a variety of perspectives, will reflect the characteristics of the individuals

contributing to it. In general, these people have selected themselves during the early phases of the Collaboration's development. The community of people who have experience preparing systematic reviews of the effects of healthcare remains small, and among those who have this experience, only some will wish to commit themselves to taking on the substantial commitment that is expected of anyone who joins the Collaboration. In other words, the disincentives that confront those who are wondering whether they should become involved are a useful screening test in themselves. To help ensure the integrity and perceived integrity of Cochrane Reviews the Collaboration has adopted a Code of Conduct for Avoiding Potential Financial Conflict of Interest. Reviewers must avoid financial conflicts of interest and disclose conflicts of interest that cannot be avoided. All reviewers must sign statements of responsibility and conflict of interest. The editorial team of each Collaborative Review Group must also disclose any potential conflict of interest that they might have. Healthcare consumers and other users of Cochrane Reviews must be involved in developing reviews to help ensure that Reviews are targeted at problems that are important to the people; take account of outcomes that are important to those affected; are accessible to people making decisions and adequately reflect variability in the values and conditions of people.

The Cochrane Handbook is the Collaboration's most tangible manifestation of the development of standards and guidelines. Beyond what is found in the Handbook, each CRG must make decisions about standards and guidelines specific to the nature of the healthcare problems within their scope. It is neither feasible nor desirable to dictate the decisions that a reviewer should take. These will vary from review to review depending on the topic, the nature of the available evidence and the resources available to the reviewer.

However, in general, the validity of Cochrane Reviews is ensured by:

1. Searching as thoroughly as possible for studies meeting the inclusion criteria of a review, relying as much as possible on centralised efforts to assist with this and ensure the thoroughness and efficiency

with which RCT's are identified

- 2. Use of explicit criteria for selecting trials for inclusion in a review and for assessing the quality of included trials*
- 3. Application of these criteria by more than one reviewer where appropriate and feasible, to ensure the reproducibility of the judgements that are made*
- 4. Ongoing efforts to collect missing information that might contribute importantly to a review, to the extent possible depending on the availability of resources and data*
- 5. Collection of individual patient data from trialists where appropriate and feasible, to the extent possible depending on the availability of resources and data*
- 6. Use of appropriate statistical techniques, where appropriate, to synthesize results*
- 7. Use of sensitivity analyses to test the robustness of the results of a review relative to any judgements or assumptions*
- 8. Cautious use of subgroup analyses and avoidance of over-interpretation of any sub-group analyses that are undertaken*
- 9. Carefully drawn conclusions, including implications for practice and future research, based on cautious interpretation of results - taking into account the limitations of the review and variability in the values and conditions of those making decisions*
- 10. Full reporting of the materials and methods used in undertaking the review*

Review Manager (RevMan) is designed to assist reviewers in constructing reviews in a structured format and one way in which the software contributes to ensuring the validity of Cochrane Reviews is by facilitating registration of a priori protocols for planned reviews.

Cochrane Centres are responsible for developing training materials and organising training workshops for CRGs and each CRG is responsible for ensuring that the members of the group have adequate training and methodological support. CRG editors need skills related to the area covered by the review group, skill and experience in critically appraising

studies of the effects of healthcare and an ability to edit scientific material for publication

It is important to have efficient arrangements for criticising the reviews prepared by contributors to the Cochrane Collaboration, and for amending reviews in the light of valid criticisms. The Cochrane Collaboration aims to create an iterative system through which successive versions of each review will reflect not only the emergence of new data, but also valid criticisms, solicited or unsolicited, from whatever source.

There are no standard methods for refereeing systematic reviews. However, several general principles merit mention. First, peer review can be useful for several stages of the review process: question formulation, protocol development, and completion of the review and updating. Second, peer review should include multiple referees or editors with both methodological and topical expertise, and with differing viewpoints. Some of the peer reviewers or referees should be external to the CRG from which the review originates. Referees should include people without direct financial, intellectual or personal conflicts of interest concerning the topic being addressed. Third, explicit standardised methods and checklists aimed at ensuring comprehensiveness and limiting bias should be encouraged among peer-reviewers. Fourth, peer review should be constructive, courteous and timely.

The main issues to consider at question formulation are whether: a) there is any overlap or potential duplication of effort with another reviewer either within or outside the originating review group; b) objectives are clearly phrased and include all of the components of well-formulated questions; and c) the review is likely to be feasible.

Reviewing protocols is more time-consuming, and is done to ensure that background information is rational and clearly presented, and that appropriate methods are planned for identifying, collecting and synthesising data. Peer review at this stage is particularly important to prevent methodological errors that may not be easily remediable at later stages of the review.

Peer review at review completion includes a second critique of the

review's methods as well as a critique of the actual results, presentation of results, discussion, and conclusion. Critiques of completed reviews are best done by multiple individuals, some of whom are external and independent of the CRG.

Preparing a review involves judgements at each step in the review process. Checklists are available for peer reviewers to use as guides for detecting important errors in the review process e.g.

Problem Formulation

- ☐ *Are review questions well formulated with specified key components?*
- ☐ *Were major changes in review questions avoided during the review process?*

Study Identification

- ☐ *Is there a thorough search for relevant data using appropriate sources?*
- ☐ *Are there unbiased explicit searching strategies that are appropriately matched to the question?*

Study Selection

- ☐ *Are appropriate inclusion and exclusion criteria used to select articles?*
- ☐ *Are selection criteria applied in a manner that limits bias?*
- ☐ *Are major changes in selection criteria avoided during the review process?*

Appraisal of Studies

- ☐ *Is the validity of individual studies addressed in a reliable manner?*
- ☐ *Are important parameters (e.g., setting, study population, study design) that could affect study results systematically addressed?*

Data Collection

- ☐ *Is there a minimal amount of missing information regarding outcomes and other variables considered key to interpretation of results?*

Data Synthesis

- ☐ *Are important parameters, such as study designs, considered in the*

synthesis?

- ☐ *Are reasonable decisions made concerning whether and how to combine data?*
- ☐ *Are results sensitive to changes in the way the analysis was done?*
- ☐ *Is the precision of results reported?*

Discussion

- ☐ *Are limitations of studies and the review process stated?*
- ☐ *Are review findings integrated within the context of relevant indirect evidence?*

Conclusions

- ☐ *Are conclusions supported by the data reviewed?*
- ☐ *Are plausible competing explanations of observed effects addressed?*
- ☐ *Is evidence appropriately interpreted as inconclusive (no evidence of effect) or as showing a particular strategy did not work (evidence of no effect)?*
- ☐ *Are important considerations for decision makers identified, including values and contextual factors that might influence decisions?*

When registering a systematic review with the Cochrane Collaboration, reviewers agree to keep it current. Keeping a review up-to-date entails repeating, at periodic intervals, the steps involved in the original review. The most logistically demanding aspect of keeping a review up to date is the identification of new studies. For CRGs that are sufficiently organised and funded, the periodic identification of relevant new studies is an ongoing function of the group's coordinator or search coordinator. At a minimum, strategies to identify new studies should include periodically checking the CRG's trials register, CCTR and MEDLINE. Original data collection forms should be used to abstract new research evidence. If new research evidence addresses important variables that were not included in original collection form, forms may be modified. In such instances, reviewers may need to recheck whether any of their earlier identified studies had such information that was overlooked.

How often reviews need updating will vary depending on the

production of valid new research evidence. At a minimum, updates should be considered on an annual basis. Even if no substantive new evidence is found on annual review and no major amendment is indicated, the date of the latest search for evidence should be made clear in the search strategy section of the review.

The San Francisco Cochrane Center is spearheading the development of a Criticism Management System for CDSR to facilitate criticism and response to criticisms of Cochrane Reviews. (Mulrow and Oxman 1997j).

4.6.2 Commentary: So members of the Cochrane Collaboration, have in general, selected themselves to contribute to the production of Systematic Reviews and the Collaboration then uses explicit methods to produce reliable and trustworthy reviews of a guaranteed minimum standard. The Cochrane Collaboration has mechanisms for maintaining and raising the standards of reviews published in the Cochrane Library including attracting dedicated participants, consumer involvement, access to studies and unpublished data, developing guidelines, using rigorous review methods, software development, training and open peer review and updating reviews. This section of the thesis is especially interested in the last mechanism described and which will be considered in some detail.

Efficient arrangements for criticising reviews prepared by Cochrane Collaborators, and for amending reviews in the light of valid criticisms are important parts of the Cochrane Collaboration structure. Peer group review takes place under the control of the appropriate CRG Editorial group in respect of:

1. Question formulation, protocol development, completion of the review and updating.
2. Includes multiple referees with appropriate methodological and topical expertise.
3. Using explicit standardised methods and checklists to ensure comprehensiveness and limitation of bias

4. And peer review should be constructive, courteous and timely.

4.6.3 The Cochrane Musculoskeletal Group – Back Subgroup Editorial Comments and Criticisms.

Question formulation, protocol development and review completion on 'The effectiveness of TENS in chronic low back pain' was subjected to peer review by three editors from the Back Subgroup of the Musculoskeletal Group of the Cochrane Collaboration. Question formulation and protocol development were reviewed and approved without further changes on the 21st November 1995. The completed Cochrane Review was subsequently submitted to the editorial team for peer review at the end of July 1996. A report from the editorial team was prepared on the 20th September and this raised several concerns, which needed to be addressed before resubmission of the review for further editorial approval.

The main areas of concern for the editorial group described in the editorial letter was as follows:

Search strategy:

- dates of search not included

Included studies:

- criterion for including studies was unclear
- other studies showing long-term response have not been included in the review
- unclear why no attempt was made to mask the names of authors, institutions, journals, or results during study selection process

Outcomes:

- the graphs reflected a very short time effect – three days to test pain was too short for a chronic patient
- patient functional status and return to work were not included

Analysis:

- separate analysis on operated vs. non-operated patients should have been conducted

- positive results on ALTENS were based on 30 patients only
- primary data was misrepresented
- inclusion of data from uncontrolled studies were included to support main findings of review

Quality assessment:

- quality of studies was not presented explicitly and was not adequate for reviewing a review.

In addition, several pages of further comments on the above and other issues, from each of the three reviewers (i.e. 29 pages in all), were appended to the above letter for further consideration! It soon became obvious that although there were several relevant issues to address there were also many comments that could not be substantiated as relevant to this review and therefore the editorial decisions were challenged as indicated below.

4.6.4 Action taken to 4.6.3: A telephone conference was set up between the author of the review, the coordinator of the Back Subgroup of the Musculoskeletal Group of the Cochrane collaboration and the co-ordinating editor on the 11th October 1996 in order to discuss and challenge the issues in contention and to arrive at a consensus opinion. The review was then revised, resubmitted and accepted into the Cochrane Library **as the first completed review in the Back subgroup**, December 2 1996 issue, in line with agreements accepted during the telephone conference as follows:

Search strategy:

- dates of search not included- *now included*

Included studies:

- criterion for including studies was unclear – *redone as requested*
- other studies showing long-term response have not been included in the review – *all exclusions were now fully discussed in the text*
- unclear why no attempt was made to mask the names of authors, institutions, journals, or results during study selection process – *this issue was now fully discussed in the text*

Outcomes:

- the graphs reflected a very short time effect – three days to test pain was too short for a chronic patient– *this issue was now fully discussed in the text*
- patient functional status and return to work were not included – *now included and studies re-reviewed in the light of this requirement albeit not part of the original protocol.*

Analysis:

- separate analysis on operated vs. non-operated patients should have been conducted– *this issue was now fully discussed in the text*
- positive results on ALTENS were based on 30 patients only– *this issue was now fully discussed in the text.*
- primary data was misrepresented – *now excluded from the text*
- inclusion of data from uncontrolled studies was included to support main findings of review – *now excluded from the text.*

Quality assessment:

- quality of studies was not presented explicitly and was not adequate for reviewing a *review* – *now included and studies re-reviewed by the two reviewers in the light of this editorial requirement albeit not part of the original accepted protocol.*

Individual comments from each editor were also addressed as described below.

Comments from Editor 1:

- Major comments: All the major comments were addressed in the text in line with this section of the editorial review.
- Minor comments: All the minor comments were addressed in the text in line with the editorial review including the “neutral tone”.
- Overall conclusion: All the comments in the conclusion were addressed in the text in line with the editorial review apart from those comments which are addressed to the management of the Editorial Back Subgroup. These comments related to the lack of appropriate editorial checklists for peer reviewers, this has now been rectified in

the latest copy of the Cochrane Handbook and as shown in the text above.

- Addendum: The five trials identified in the editors addendum for inclusion in the review were **not included** as they did not meet the inclusion criteria and this was now discussed in full in the text and under the “Characteristics of excluded studies” section of the Cochrane Review.

Comments of Editor 2:

- The comments of editor 2 are entered in the margins of the text: All major and minor comments were addressed in the text in line with this section of the editorial review including the quality issues.

Comments of Editor 3:

- The comments to authors from Editor 3 was described in eleven sections: All major and minor comments contained in the eleven parts of this section were addressed in the text in line with this section of the editorial review and also in the light of the following observations.
 - Comment 1: the exclusion of the trials of Lehmann 1983/1986 and Herman 1993, which were not trials of either conventional TENS or ALTENS, were now dealt with fully in the text with the compelling reasons requested.
 - Comment 2: the blinding of reviewers was now fully dealt with in the text, data was extracted by three reviewers - J G Gadsby, Dr M Flowerdew and Professor Alan Bennett and a single reviewer (J G Gadsby) co-ordinated the data. Three reviewers in all. However, Professor Alan Bennett had to withdraw, after the initial data extraction had been completed, but before the analysis etc could take place, from the team of reviewers for personal and commercial reasons, which were not related to the conduct of this research. His major contribution was to the protocol and this was acknowledged at the time and a further acknowledgement on the cover sheet is now included.

- Comment 3: uncontrolled trial data were removed from the review in line with the editorial comments, although this requirement could be argued against!
- Comment 4: the issues raised here were now dealt with fully in the text including new references to support the observations.
- Comment 5: the authors have reviewed all the studies again in the light of these comments and have produced a Quality Index in line with the recommendations made here.
- Comment 6: the issues raised here have now been dealt with fully in the text. The studies in our review may have the lowest ratings in other reviews but they do have the highest rating in ours (and we consider this to be correct), the results of this review are based on the specified criterion outlined and accepted in the protocol and any excluded data is on the basis that it does not meet our inclusion/exclusion criteria, and obviously this data is not considered as high quality and excluded from the review, and the rationale is therefore most clear.
- Comment 7: the issues raised here were dealt with fully in the text, including the observations on ankylosing spondylitis subjects which are also included in other trials with non-specific back pain subjects see e.g. Marchand 1993. We stand by our comments on Deyo's study and the editor has based his/her observations on incorrect numbers combining TENS subjects with TENS and exercise subjects, and Sham TENS with Sham TENS and exercise subjects, which is hardly comparing like with like. The question of model validity is now fully discussed in the text.
- Comment 8: it is unclear in the Cochrane Collaboration Handbook which graphic presentation to choose to represent the odds ratios in this situation and the editorial team failed to give me any direction on this matter... in the absence of any advice on this I have gone for 'improvement' [note recommendations in support of this point in the new version of the Cochrane Handbook]

- Comment 9: the issues raised here were dealt with fully in the text after re-reading the studies concerned, this may be an omission on the part of the authors but it should have been raised at the protocol acceptance stage, however, in the studies under consideration in this review these two outcomes (functional status and return to work) did not play a significant role, albeit important though these outcomes are.
- Comment 10: the issues raised here were dealt with fully in the text including modifying the optimistic tone of the review in accordance with the instructions of the editorial team.
- Comment 11: no suitable comments on this observation are possible which read “ if this analysis were published and disseminated as is, the message to every pharmaceutical and device manufacturer would be clear: in order to win at the ‘meta-analysis game’ one needs only to fund multiple small flawed studies with design features favouring the new treatment. These would numerically overwhelm large well-designed studies and could result in favourable meta-analysis. This would be an unfortunate conclusion and message”.

Comments on the Checklist Sheet for Reviewing a Protocol:

We share the editors comments on the suitability of this checklist for reviewing a review nevertheless the issues raised here were now dealt with fully in the text (see also comments on editor 1- overall comments above).

A letter to the editorial team was also enclosed with the completed review and the main issues covered were as follows. *“The enclosed review both in hardcopy and electronic media would now appear to meet the requirements of the editorial review as outlined in their commentaries and as discussed above and in the main text of the review. I trust that this update of the review, in line with the recommendations of the Editors, now meets the requirements of the Cochrane Collaboration, Back Subgroup of the Musculoskeletal Group, and I look forward to its inclusion in the Cochrane Library in due course. However,*

I feel inclined to make the following observations on the tone of this editorial review which hardly seems to be one of 'collaboration' to me, and other readers, but appears more like one of 'confrontation', which is surely not one of the objectives of The Cochrane Collaboration as described in the Handbook, on electronic media and other CC literature. Whilst we agree that most of the comments are indeed most helpful, and hopefully they have contributed to improving the quality of this review, there are others, however, which are in our opinion, absolutely incorrect and these are dealt with in the text of this review. It is also a sobering thought that the two reviewers of this Systematic Review are content area experts, who have spent the last fifteen to twenty years treating many conditions, on a daily basis, with TENS, ALTENS and EAP, including chronic low back pain, and so it is not just an academic exercise in reviewing the literature but also a reflection of the expertise of the contributors, and hopefully not their biases - which has been observed for, and monitored by, members of the academic supervision team for this review".

It is now noted that several of the above comments would appear to have been taken into account, as indicated in the text above, in the construction of the latest version of the Cochrane Handbook (1997), not least the arrangements for criticising reviews prepared by Cochrane Collaborators, and for amending reviews in the light of valid criticisms which should now include multiple referees with appropriate methodological and topical expertise, using explicit standardised methods and checklists to ensure comprehensiveness and limitation of bias and that peer review should be constructive, courteous and timely.

This may be in some small way a response to a copy of the above letter, which was also submitted to Iain Chalmers of the UK Cochrane Centre as the Chief Coordinator of the Cochrane Collaboration, and his reply included the following:

"Thank you for sending me a copy of your letter. During my travels I had an opportunity to look through all the material you sent me.

I have to say that I agree with many of the points raised by the referees, who had clearly gone to some trouble to look through your review carefully, and I am glad that you have dealt with them. I agree with you that some of the comments made by the referees did not appear to take into account to act on them would have resulted in breaches of protocol, which had been through an editorial review process. Like you, I was sorry that suggestions for improving your review were not communicated to you in a more friendly and positive way. One of the things which you need to understand, however, is that many of the editors working within the Cochrane Collaboration have been editors of traditional medical journals. In traditional journals there is no need to make any attempt to build a team of contributors, as is required for Cochrane groups. There is a cultural difference which will need to be recognised by everyone involved, but adaptation to a new style of interaction is bound to take some time, and there will be misunderstandings and hurt feelings along the way. It seems to me that you and the editors in your group have probably established the basis of mutual respect in future and I do hope that this is the case..."

These issues were subsequently raised at the 4th International Cochrane Colloquium held in December 1996 in Adelaide Australia and new guidelines were issued as described above. It is to be hoped that in future all reviewers will benefit from the experiences of this review process and thesis construction in order that even higher quality reviews will be completed.

On January 21st 1997 confirmation that this review on 'The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of chronic low back pain' had been accepted in to the Cochrane Library and was also to be the first completed review in the Back subgroup, was received from the coordinator of the Back Subgroup of the Musculoskeletal Group of the Cochrane Collaboration.

4.6.5 A New Criticisms Management System:

The New Criticism Management System for CDSR to facilitate criticism and response came on line in the April 1997 (Issue 2) release of the Cochrane Library.

"Through seeking we may learn and know things better. But as for certain truth, no man has known it, for all is but a woven web of guesses". Xenophanes, 6th century BC.

This issue of The Cochrane Library introduced a new system for submitting comments and criticisms on Cochrane reviews and protocols. This system consists of a series of screens (and help screens) for entering the comments/criticisms in a highly structured form, followed by options for either transmitting the comments via the Internet, or printing them to be sent by fax or regular mail. The Cochrane Collaboration gladly accepts comments on protocols, as well as reviews, because these can reveal weaknesses at a time when corrections can be made more easily. Comments on protocols provide a form of pre-publication review, while comments on Cochrane Reviews provide for ongoing post-publication review.

How the feedback will be used:

Future issues of the Database will display summaries of the feedback received for each review in a new section 'View Comments and Criticism' (to be listed just after the 'Conclusions' section). The authors of the review will respond to the feedback sent by users to their reviews in a well-considered and timely fashion. The authors' responses will be displayed along with the comments, and the names of those submitting criticism will be acknowledged. An archive of the full text of the feedback may also be available.

The Cochrane Collaboration does not accept anonymous criticism based on the following assumptions:

1. Users who send in feedback should take responsibility for their comments.
2. Users who send in feedback should receive public, named recognition.

tion in what will be the new 'View Criticism' section of Cochrane reviews for the substantive feedback they submit to improve the quality and usefulness of the reviews.

3. It is important that authors be able to contact the users, either because the transmission of the comments was defective or because the authors need further clarification about the users' feedback.

At the time of writing (01/98), the author of this review has not received any direct comments or criticism from users of the Cochrane Library via the official Comments and Criticisms mechanism but he will of course respond quickly to any forthcoming ones and/or as requested by the Criticisms editor of the Back Subgroup.

4.6.6 Comments and Criticisms received from the Criticism Editor for the Cochrane Back Subgroup:

Note: In view of the large number of comments and criticisms in this subsection the author has addressed each one immediately following the comment under '**Action**'. The action taken was conveyed by letter to the Criticisms Editor for the Cochrane Back Subgroup and will also be used in maintaining and updating this review in due course.

The day following the initial writing of the last paragraph of section 4.6.5 (14.5.1997) a letter arrived from the new Criticism Editor for the Cochrane Back Subgroup and the letter went as follows:-

"I am writing to you as Criticism Editor for the Cochrane Back Subgroup. This is a new role within the Cochrane Collaboration, aiming at organising and summarising post-publication criticism of reviews from users of the Collaboration Library and to oversee and negotiate with reviewers their replies to these criticisms. Quite a mouthful, but think of me as a liaison between people who criticise reviews and the reviewers themselves.

The review that you and Dr Flowerdew wrote on the effectiveness

of TENS and ALTENS in the treatment of patients with chronic low back pain has been on the CDSR since January 1997. Already we have had some comments on your review. I therefore would like you to read these comments as listed below, and let me know what you envision would be the proper strategy in dealing with these criticisms. I think some of these problems can be dealt with rather easily in an update of the review, other points might take more time and consideration”.

Note: It is interesting to note here, that in response to my enquiry, no Comments or Criticisms had officially been received by the San Francisco Cochrane Centre in respect of this Cochrane Review, at the end of July 1997, which makes one speculate that the comments and criticisms received from the Criticisms Editor are in fact a re-hash of some old and new editorial comments, an observation which will become clearer as we work through the letter.

Comment 1. *“In the introduction section it should be added that there are only 6 RCT’s which truly provide efficacy data (as opposed to the 600 publications that are mentioned). The statement that the ‘technique of systematic reviews (SR’s) would provide definitive answers’ is quite strong. I think SR’s can not be thought of as a panacea for everything, and since only six trials are analysed here it seems somewhat overstated”.*

Action:

a. It is correct that here are only 6 RCT’s which in the opinion of the authors truly provide efficacy data out of the 70 studies on chronic low back pain which were identified during the initial and subsequent search strategies. These 70 studies are a subset of more than 600 publications (covering all clinical applications of TENS/ALTENS and other electrostimulation techniques) identified by Nolan (1991) together with the subsequent publications from the period 1991-1997.

b. 'In order to provide a clearer assessment using a systematic review and meta-analysis' might in fact be a more appropriate description of our objectives.

Comment2. "There is concern on the exclusion and inclusion criteria in this review. For instance, it seems as if it is clear to you and Dr Flowerdew which stimulation modalities are effective (or correct) and which are not, and several trials are therefore excluded. Also criteria such as the definition of chronicity (8 weeks), credibility of placebo and FDA approval status are not always explicit. All in all, in the description of the included studies new exclusion criteria appear, which are not in your method section. This problem could be dealt with by stating the exclusion criteria more explicitly and being more clear in the excluded studies table.

Also, please check the trials by Lehmann, Melzack 1980, Hermann, Lundeborg, Sodipo, Tulgar 1991b, and explain why the study by Marchand (not truly randomised) was included".

Action: The authors, both content area experts and full-time electrotherapy practitioners with more than fifteen years of experience each, both work on a daily basis with the techniques of electro-stimulation, electroacupuncture, ALTENS, TENS and other related modalities in the treatment of a wide range of disorders. The inclusion/exclusion criteria for studies in respect of the stimulation modes were based on the electrical parameters described by Mannheimer and Lampe (1984:339-41) as follows:

- a. Conventional TENS using a high rate, narrow pulse and moderate stimulation with parameter adjustments for rate between 50 to 100Hz and a low pulse width from 40 to 75 microseconds with an intensity raised to the level of comfort.
- b. Acupuncture-like TENS (also known as "strong low rate (SLR) TENS – Robinson 1996) with electrical parameters adjusted to provide a low rate (1 to 4Hz), a wide pulse width between 150 to 250 microseconds with an intensity at as high a level as can be toler-

ated by the patient.

- c. Other less used and little researched modes such as subsensory stimulation, noxious level stimulation, burst train and modulated forms of electrical stimulation were not considered for inclusion in this review.

So more recent publications confirm that the above selected recommended parameters are correct (Robinson 1996:209 and see also Walsh 1997:36-7).

The decision to base the inclusion criteria for chronicity above 8 weeks was made on the basis of evidence presented by among others, the CSAG (1994) Back Pain Report which suggests that the first six weeks are crucial in preventing chronicity, whereas 90% (CSAG 1994:55,61, van Tulder 1996:1) of patients will have recovered by this time. The conventional classification of non-specific low back pain as acute <6 weeks duration, subacute <12 weeks duration, and chronic > 3 month duration ignores the dynamic nature of this recurring condition and most researchers define non-specific low back pain by the duration of pain, although there is no standard definition of the terms (Evans and Richards 1996). Therefore, on this basis, studies were included if they reported on a mix of sub-chronic (six to twelve weeks) and chronic low back pain patients (above twelve weeks). Studies were excluded if they reported on acute (six weeks or less) low back pain patients or studies with a mix of acute and chronic low back pain patients. These inclusion/exclusion criteria are also in line with those of van Tulder *et al* (1996:247).

The criteria in respect of credibility of placebo rests on the similarity of the control treatment to the active treatment, which may pose difficulties for some sensory therapies such as acupuncture and high level stimulation. However, the use of a creative, and what appears to be a fully functioning TENS unit with flashing LED's etc but with no electrical output to the electrodes, rather than just a dead battery placebo, would appear to be the ideal. Patients receiving sham therapy should also receive visit frequency, contact and support equivalent to

that in the active therapy condition (Turner 1994).

The criteria for Food and Drug Administration regulations relates to any units not authorized for marketing within the USA and applied to the CODETRON unit at the time of initial preparation of this review and as used by Hermann 1993. This study was a randomized controlled trial of a 'novel' transcutaneous electrical nerve stimulator called "CODETRON" which did not meet the electrical parameters of this review and furthermore was applied in a rehabilitation programme for acute occupational low back pain. The FDA did not permit the sale of this unit before 1995 as it was classed as an experimental device (Pomeranz 1996 – its designer!).

N.B. The Food and Drug Administration (FDA), is a USA federal agency responsible for the enforcement of federal regulations regarding the manufacture and distribution of food, drugs, and cosmetics as protection against the sale of impure or dangerous substances. (Mosby 1994).

The exclusion criteria may now be stated more explicitly as:

1. All randomised controlled trials which failed to compare an active conventional TENS or acupuncture-like TENS with a credible placebo treatment.
2. All studies which failed to meet the recognised electrical parameters for high frequency ($>10\text{Hz}$) low intensity stimulation parameters of conventional TENS or low frequency ($<3\text{Hz}$) high intensity stimulation (also known as "strong low rate (SLR) TENS) parameters in the treatment of chronic low back pain.
3. All other studies which described less used and little researched modes of transcutaneous electrical nerve stimulation such as sub-sensory stimulation, noxious level stimulation, burst train and modulated forms of electrical stimulation.
4. Studies were also excluded if they reported on acute (six weeks or less) low back pain patients or studies with a mix of acute and chronic low back pain patients.
5. All uncontrolled and non-randomised studies of TENS and chronic

back pain.

6. All descriptive studies of TENS and chronic low back pain.

We have rechecked the excluded studies table and the authors of this review consider that the descriptions of excluded studies given in this section are now more than clear in the light of the more explicit exclusion criteria described above. We have also rechecked and reviewed the following trials by Lehmann 1983/1986, Melzack 1980, Hermann 1993, Lundeborg 1984, Sodipo 1981 and Tulgar 1991b and cannot find any new evidence to support the inclusion, of any of these six studies in this review and meta-analysis, for the reasons described in the table of excluded studies.

The study by Marchand (1993) has been criticised for not being “truly randomised” i.e. a pseudo-randomisation with some matching of subjects and symptoms was described, however, this study was included in this review in view of its strengths and quality index as described in the text and we can see no valid reasons to exclude it. The reader may also be interested in the following recent critiques on Marchand (1993), see Robinson (1996) and Walsh (1997) which generally support the conclusions found in this Cochrane Review. However, a sensitivity testing on the results of the meta-analysis was carried out by removing the Marchand (1993) study in order to assess the influence of this study on the meta-analysis and the results were as follows: The original meta-analysis for comparison 1. (TENS vs. placebo) gave an OR of 1.52(95%CI, 0.90,2.58) and for Comparison 3. (TENS/ALTENS vs. placebo) an OR of 2.11 (95%CI, 1.32,3.38). A new meta-analysis which excluded Marchand 1993 for comparison 1, (TENS vs. placebo) gave an OR of 1.39(95%CI, 0.80,2.46) and for Comparison 3, (TENS/ALTENS vs. placebo) an OR of 2.03(95%CI, 1.25,3.32). These results indicate that the inclusion of the Marchand (1993) study in this review did not significantly affect the results of the original meta-analysis when an exclusion of this study was made during sensitivity testing.

Comment 3: "The reason why you did not blind the evaluation seems unconvincing".

Action: There were few guidelines available on blind assessment at the time of protocol submission (November 1995) and at the commencement of this review. Furthermore, more recent guidelines taken from the Cochrane Handbook (1997) recommend that "Reviewers must also decide whether those assessing study validity will be blinded to the names of the authors, institutions, journal and results of a trial when they apply critical appraisal criteria to the methods. Some empirical evidence suggests that blind assessment of reports might produce lower and more consistent scores than open assessments. However, such assessments are very time consuming. Reviewers must weigh the potential benefits of blind assessments against the costs involved in deciding whether or not to blind the reviewers. Further research is underway comparing blind and open assessments of trial validity and these results may help guide this decision. Until we have firm guidelines from the Cochrane collaboration on this aspect of reviewing studies we decided to use the guidelines of Blair (1995). "Bias can arise during study selection or data extraction if analysts show subjective preferences for including studies or data elements within studies. For example, bias may derive from preferences based on a consideration of who the author is or on the study outcome rather than on more objective assessments of study eligibility and data relevance. The need to overcome bias in the selection of studies and in the extraction of data can be partially addressed through development and use of explicit criteria and procedures for selection and extraction" (Blair 1995) and this we have aimed to do in this review.

On the subject of blinding reviewers to studies for analysis the recommendations were that "Blinding of all identified studies that are candidates for analysis, is not necessary and in general should be discouraged. In many instances, for example, large studies result in several publications, all of which may repeat various analyses. Blinding

would then make it difficult to recognise reports that were from the same study rather than individual studies, and important information needed for stratification in the meta-analysis could be lost” (Blair 1995).

It was suggested by Moher (1996a) that 10 years ago the quality of clinical reports should be assessed under masked conditions and quoted Chalmers et al. (1983) in support of this. However, the only reference to masking we can find is contained in the following extract, “The first tabulation of risk factors and case-fatality rates was unblinded – i.e., it was done with knowledge of how the treatment assignment was carried out. The second was blinded – i.e., it was done after the pertinent assignment data had been obliterated in the photocopy” but no further reference to a recommended practice. Preliminary results from a recent study, Jadad-Bachara (1996) suggests that trial quality should be assessed under masked conditions in any context in which quality judgements play a role in decision making. In this study two groups of judges allocated randomly to conduct the assessments under masked or unmasked conditions assigned scores to the same set of articles and found that masked assessments of the reports produced significantly lower and more consistent scores than open assessment. It is understood from this paper that J Berlin and colleagues are also assessing whether the results of masked assessments of trial qualities affect the overall results of systematic reviews. However, there does not appear to be a definitive answer to the question of masking at this stage and especially at the protocol and review development stages of our Cochrane review and we therefore await the results of these further studies which will hopefully give us more explicit guidelines to follow. Having just finished writing the above paragraph I find that Berlin (1997) had just published the results of their study, to determine whether meta-analyses conducted with readers blinded to identifying information produce systematically different results than those same meta-analyses conducted with unblinded readers. This randomised controlled trial found that blinding during study selection

and data extraction had neither a clinically nor a statistically significant effect on the summary odds ratio for the sample of five meta-analyses under investigation. The time involved in preparing and blinding papers was extensive and they conclude that blinding is not necessary when conducting meta-analyses of randomised clinical trials (Berlin 1997).

Comment 4. "The duration of treatment effects deserves more attention. It seems as if all studies with no follow-up were the ones delivering significant effects, So, it seems there is no insight in long term effects. Please state likewise in the abstract and in the conclusions".

Action: The follow-up in the six studies under review were rather diverse and mostly for a very short time, at the end of treatment in four, at three and at three and six months in two. The long term follow up by Deyo 1990 at three months and of Marchand 1993 at three and six months showed a near return to baseline conditions. There is therefore, little evidence to support the long-term effects of TENS/ALTENS in the treatment of chronic low back pain in the studies assessed. Further studies need to be done, mostly because of the lack of availability of proper studies in this field, which also reflects the lack of suitable follow-up studies at three and six month intervals, and this is reflected in the recommendations section of this Cochrane Review.

Comment 5. "In the Deyo study (Table 2) only 30 patients/group are reported. Since this is a cross-over study, the proper comparison (TENS vs. sham TENS) would be 60 and 65 patients respectively. Please correct this and adjust the (probably altered) outcomes as well".

Action: The Deyo 1990 study is not in fact a cross-over study but a randomised controlled trial with four comparison groups, i.e. a TENS group of 36, a Sham TENS group of 36, a TENS and exercise group of

37 and a Sham TENS and exercise group of 36 - before dropouts. It is interesting to note that the following recent critiques on Deyo 1990, (Robinson 1996, and Walsh 1997), came to similar conclusions and reservations as the authors outlined in this Review.

This systematic review and meta-analysis intended to pool only the TENS group and the Sham TENS group and to exclude the two exercise groups on the basis of not comparing 'like with like' treatments'. On examining the data sheets, in response to the readers comments/criticisms, we found that the original meta-analysis was in fact based on combining the TENS and TENS plus exercise groups together and the Sham TENS and Sham TENS plus exercise groups together. Therefore the results of the meta-analysis stand and do not require correction. However, if we now conduct a second meta-analysis based on the two groups of TENS and Sham TENS without combining with the exercise groups the meta-analysis outcomes are as follows:

1. The original meta-analysis for comparison 1, (TENS vs. placebo), gave an OR of 1.52(95%CI, 0.90,2.58) and for Comparison 3, (TENS/ALTENS vs. placebo) an OR of 2.11 (95%CI, 1.32,3.38).
2. A new meta-analysis which includes only the TENS and Sham TENS groups of Deyo 1990 for comparison 1, (TENS vs. placebo) gave an OR of 1.72(95%CI, 0.92,3.20) and for Comparison 3, (TENS/ALTENS vs. placebo) an OR of 2.54(95%CI, 1.49,4.31). These results indicate that the exclusion of the exercise groups, of Deyo 1990 study, enhances and strengthens the results of the original meta-analysis.

Comment 6. "It seems that the outcomes on efficacy of TENS are not statistically significant (apparent from the overlapping confidence intervals). Therefore the conclusions of this review could perhaps be interpreted differently by the readers than by the authors".

Action: A secondary examination of the "Metaview' charts (Figure XXV) for comparisons 1, 2, 3 and 5 suggests that the results may be interpreted as follows:

- Comparison 1: TENS vs. Placebo in pain reduction. The right side of the figure shows that the effect of TENS treatment for chronic back pain was favourable in all four studies, but did not reach statistical significance (apparent from the overlapping of the unitary line by their confidence intervals). The overall pooled estimate of treatment effect given at the bottom of the chart favoured TENS treatment for reducing chronic low back pain, at least in the short term, and almost reached significance (with the lower limit of the confidence interval at 0.90 or 0.92 if we use the meta-analysis as discussed in section 5 above). These interpretations are based on relatively small numbers of subjects i.e. 227, but nevertheless represents the best available evidence we have at the time of writing.
- Comparison 2: ALTENS vs. Placebo in pain reduction. The right side of the figure shows that the effect of ALTENS treatment for chronic back pain was favourable in both studies and were statistically significant (with no overlapping of the unitary line by their confidence intervals). The overall pooled estimate of treatment effect given at the bottom of the chart yielded a definitive significant combined effect estimate which indicated strongly that ALTENS treatment is effective for reducing chronic low back pain, at least in the short term. These interpretations are, however, based on a very small number of subjects i.e. 61, but nevertheless represents the best available evidence we have at the time of writing.
- Comparison 3: TENS/ALTENS vs. Placebo in pain reduction. The right side of the figure shows that the effect of TENS/ALTENS treatment for chronic back pain was favourable in all six studies, but in only two was statistical significance achieved. The overall pooled estimate of treatment effect given at the bottom of the chart yielded a definitive significant combined effect estimate which indicated strongly that TENS/ALTENS treatments are effective for reducing chronic low back pain, at least in the short term. These interpretations are, however, based on relatively small numbers of

subjects i.e. 288, but nevertheless represents the best available evidence we have at the time of writing.

- Comparison 5: ALTENS vs. Placebo in change in Range Of Motion. The right side of the figure shows that the effect of TENS treatment in improving ROM for chronic back pain subjects was favourable in both studies and were statistically significant (with no overlapping of the unitary line by their confidence intervals). The overall pooled estimate of treatment effect given at the bottom of the chart yielded a definitive significant combined effect estimate which indicated strongly that ALTENS treatment is effective for improving ROM in subjects with chronic low back pain, at least in the short term. These interpretations are, however, based on a very small number of subjects i.e. 61, but nevertheless represents the best available evidence we have at the time of writing.
- An experimental Cumulative meta-analysis (see Figure XXV) on comparisons 1 and 3 gave the following results:
 1. Comparison 1: TENS vs. Placebo in pain reduction: The cumulative meta-analysis (CMA) gave an OR of 1.49 (1.05, 2.13) in comparison with the original meta-analysis OR 1.52(95%CI, 0.90,2.58). The 95% CI of the CMA now reaches statistical significance with no overlapping of the unitary line.
 2. Comparison 1a: TENS vs. Placebo in pain reduction (without (Deyo 1990) exercise groups): The cumulative meta-analysis (CMA) gave an OR of 1.64 (1.09, 2.47) in comparison with the original meta-analysis with an OR of 1.72(95%CI, 0.92,3.20). The 95% CI of the CMA now reaches statistical significance with no overlapping of the unitary line.
 3. Comparison 3: TENS/ALTENS vs. Placebo in pain reduction: The cumulative meta-analysis (CMA) gave an OR of 1.93 (1.50, 2.48) in comparison with the original meta-analysis OR of 2.11 (95%CI, 1.32,3.38).
 4. Comparison 3a: TENS/ALTENS vs. Placebo in pain reduction (without (Deyo 1990) exercise groups): The cumulative meta-

analysis (CMA) gave an OR of 2.29 (1.74, 3.03) in comparison with the original meta-analysis OR of 2.54 (95%CI, 1.49,4.31). The CMA shows a narrowing of the 95%CI and a significant treatment effect can be detected from as early as Jeans 1979 study. This Cumulative type of systematic review indicates that the use of TENS/ALTENS for the treatment of chronic back pain, at least in the short term, could have been shown to be beneficial almost 20 years ago.

- A Bayesian analysis undertaken by the De Montfort University's Department of Medical Statistics using the BUGS and CODA software and presented at a Statistical Issues in Biopharmaceutical Environments Conference in July 1996 and was described earlier in the thesis. They concluded that the posterior estimate for the population increase in odds of improvement on ALTENS/TENS compared to placebo was 3.86 (mid-95% credible interval 1.46 to 13.74). This result suggested a potential benefit for the use of ALTENS/TENS in the treatment of chronic low back pain. This result is not dissimilar, if somewhat stronger, than the systemic review and meta-analysis under consideration in this thesis. However, the credible interval for this estimate is extremely wide and reflects both the small number of studies and small sample sizes. This study also ends with the recommendation to run a large randomised placebo controlled study assessing the effectiveness of ALTENS/TENS in the treatment of chronic low back pain.

Suggested conclusions would now be based on the following statements:

- i. There is evidence to support the treatment of chronic back pain, at least in the short term, with TENS being more effective than placebo, but the evidence does not quite reach statistical significance unless we use a cumulative meta-analysis. There is no available evidence at this time to support the use of TENS treatment, as being more effective than placebo, in improving the range of motion in patients with

- chronic back pain.
- ii. There is evidence, which is statistically significant, to support the treatment of chronic back pain with acupuncture-like ALTENS for pain relief, at least in the short term, being more effective than placebo. There is also evidence that ALTENS treatment improves the range of motion of subjects with chronic back pain, being more effective than placebo, at least in the short term.
 - iii. There is statistically significant evidence from pooling the TENS and ALTENS data in a cumulative meta-analysis to indicate that the use of TENS/ALTENS for the treatment of chronic back pain, at least in the short term, could have been shown to be beneficial almost 20 years ago.
 - iv. There is no data available to support the notion that TENS or ALTENS is successful in returning patients to work faster than alternative treatments.
 - v. There is no difference on functional outcomes between TENS/ALTENS and Placebo
 - vi. The use of TENS/ALTENS is relatively free from side effects in comparison with a credible placebo treatment.

Comment 7. "Therefore, the abstract should be rewritten, emphasising the scant information that was derived from the studied trials".

Action: The abstract was rewritten in line with the above comments as follows:

Abstract:

Objectives: To determine the effectiveness of transcutaneous electrical nerve stimulation in reducing pain and improving function in patients with chronic back pain.

Search strategy: Electronic searches of EMBASE, MEDLINE, CISCOM,

AMED for all studies of TENS treating chronic back pain together with citation tracking.

Selection criteria: The inclusion criterion for studies included in this review, 6 out of 70, was comparisons of TENS/ALTENS versus placebo in patients with chronic back pain.

Data collection and analysis: Two reviewers extracted outcome data on pain reduction, range of movement, functional and work status, and trial design qualities.

Main results: The ratio of odds of improvement in pain for each comparison was calculated: TENS/ALTENS vs. placebo at 2.11 (95% CI 1.32, 3.38) times that of placebo, ALTENS vs. placebo at 7.22 (95% CI 2.60, 20.01) and TENS vs. placebo at 1.52 (95% CI 0.90, 2.58). The odds of improvement in range of motion on ALTENS vs. placebo was 6.61 times (95% CI 2.36, 18.55) that of placebo.

Conclusions: There is statistically significant evidence, from the limited data available, that TENS/ALTENS reduces pain and improves range of motion in chronic back pain patients, at least in the short term. There is statistically significant evidence, pooling the TENS/ALTENS data in a cumulative meta-analysis, to indicate that using TENS/ALTENS for the treatment of chronic back pain in the short term, could have been shown to be beneficial almost 20 years ago. A powerful RCT of ALTENS and TENS is now needed to confirm these findings.

Comment 8. "As you can see, it is quite a list. Yet, most of the noted criticisms could easily be solved. Please free fell to contact me on these criticisms, and let me know how you feel about them and how you will respond to them.

Please bear in mind that dealing with criticisms is a new phe-

nomenon to the Back Subgroup as well. It is therefore imperative that we deal with them properly and set a standard for the future, which is satisfactory to all parties involved.

With best wishes The Cochrane Back Subgroup Comments and Criticisms Editor”.

Final Comments: The above comments and criticisms have been addressed, as indicated in the text, in a letter (01/05/97) to the Comments and Criticisms Editor for his consideration. No reply to these comments had been received from the Editor at the time of writing this sub-section (01/08/97). A reply was subsequently received in September 1997 and the comments, criticisms, and action taken have now been used to update the Cochrane Review in time for Issue No. 2 1998. Some of the comments were indeed most helpful and necessary in order to strengthen and improve the review (and also to detect and correct some minor errors). Some of the comments had already been addressed during the initial review process and therefore no further action was taken on these issues. I now look forward to comments and criticisms from actual users of the Cochrane Library, but none have so far been received at the time of writing this updated section, at 12thth January 1998.

4.6.7 Other Comments and Criticisms Systems

In addition to the two systems described above there are other less formal, and perhaps less biased, criticism systems which are also useful to reviewers and these include pre-publication peer reviews e.g. the BMJ submission report and commentaries such as the one to be found in the Evidence-Based Medicine journal. Two of these are considered in the next sub-section and they were subsequently used to improve the Cochrane Review under discussion.

4.6.7.1 The British Medical Journal:

A paper was submitted to the BMJ in December 1996 for simultaneous publication with the Cochrane Library Review. Unfortunately, this paper was subsequently 'lost' in their system only resurfacing several months later (five to be exact), having missed the appropriate publication dates and the medical press interest in it (and in the meantime the Evidence-based Medicine Journal produced an abstract of this review). But as an assistant editor of the BMJ said to the author, seeking information and explanation for the delay in publishing his paper, "well we haven't done too well by your paper I'm afraid!"

However, the BMJ full editorial committee rejected the above article for publication on the 8th May 1997 for the officially stated reasons which are discussed below together with a copy of the referee's comments for consideration and these are also described as follows:

Action: on the Editorial comments:

1. *"Back pain is never clearly defined".*

The definition of back pain remains a difficult conundrum, there does not appear to be an accepted, or recognised method of differential diagnosis certainly at the time these studies were carried out. The recent definitions of acute, subacute, chronic and post surgery categories are now more clearly defined in the text.

2. *"In view of the poor quality of the studies available for analysis, we felt that however, important the question, this meta-analysis did not take the debate forward sufficiently for us to want to offer publication in the BMJ".*

Whilst the authors sympathise with the editorial comments in the light of events described earlier in view of the lost manuscript, it is most interesting to note the editorial comments of the Evidence-Based Medicine Journal in respect of this Cochrane review which included the following information "Its (E-BM Journal) purpose is to help keep clinicians up to date on a wide range of research by abstracting high quality articles from key journals. Your article was chosen for ab-

straction because it met (at least) these criteria:

- i. an identifiable description of the methods
- ii. indication of the sources and methods for searching for articles
- iii. statement of the clinical topic content for selecting articles for detailed review

Congratulations on your fine article". Professor Brian Hayes, McMaster University and Professor David Sackett, University of Oxford.

3. *"Insufficient evidence is provided on publication bias".*

We are not quite sure how to, or what to read into this comment in view of the earlier comments?

4. *"The extremely long list of references would benefit from shortening".*

This is perhaps a reasonable observation to make as the reference section was quite comprehensive but this is now purely academic in view of the paper's rejection

5. *"The notion of the 6 fraction list (page 10) should be explained more clearly for the general reader".*

This should in fact read "the notion of the fixed fraction myth" and was correct in the text but has obviously suffered from editorial misinterpretation and translation by the word processor. The "fixed fraction myth" relates and was properly referenced to the paper by Patrick Wall (1992). In this paper Wall discusses and rejects the popular myth that there is a fixed fraction (one third) of the population who respond to placebos by scanning a large series of double-blind responders with varying responses from close to 0% to near 100% depending on the circumstances of the trial.

Action: on the Referee's comments

1. *"This is essentially a meta-analysis undertaken on a topic where unfortunately a lot of controversies exist, but has only a few good studies available. The authors in fact had only six studies available to them for analysis, with a total of only 288 patients".*

This statement is correct and the authors agree with the sentiments expressed and therefore have no further comments to make on this.

2. *"As far as I can make out there are two important conclusions to the manuscript:*

(a) TENS and ALTENS are better than placebo in chronic back pain treatment

b. My reading of four of the refereed publications used for the meta-analysis (I didn't have access to the others) suggests that the follow-up of those studies were rather diverse and mostly for a very short time (at the end of treatment in three and at 3 and 6 months in one). The long term follow up (ref. no.18, Marchand et al 1993) showed no differences at 3 or 6 months. This important point has not been brought into sufficient focus in the manuscript. This I consider a major omission and likely to give the impression that the method of treatment discussed (TENS and ALTENS) are very useful, compared to placebo, for long term pain relief.

(b) Further studies need to be done, mostly because of the lack of availability of proper studies in this field. This point of course has been sufficiently highlighted in the manuscript".

The authors of this Cochrane Review agree with the above comments and adjustments to the text of the review to reflect this will be done for the next update.

3. *"The methodological and statistical approach used is satisfactory. The standard format of a meta-analysis was followed to a large extent; my only comment is that the authors have confined themselves to mostly English language/translation publications only. This may have undervalued the analysis considering that TENS and ALTENS are used in many other parts of the world and related publications are likely to be in other languages".*

The authors have considered this aspect, in some detail, under the response to Professor Ernst's commentary in the Evidence-Based Medicine Journal, which follows in the next sub-section of this thesis.

4. *"I was able to get hold of about half of the references quoted; there are some minor mistakes in them".*

This statement is also correct and reflects the time this referee

must have spent reading our paper, in order to detect these minor errors, for which we are most grateful and these errors have now been corrected.

5. *"There is not much attempt to explain the modes of pain relief reviewed (TENS and ALTENS) except for brief mentions".*

This statement is also correct as far as the BMJ paper goes but more details are in fact available in the Cochrane Library Review available on CD-ROM.

6. *"There is no attempt to describe the techniques used to assess 'improvement' after treatment. The techniques used were diverse (physical, VAS, MPQ, PRI) and these should have been discussed and commented upon before concluding the advantages of the methods of pain relief".*

This statement is again correct as far as the BMJ paper goes but to embark on another subject would have increased the length of the article to even greater proportions so was not included, however, more attention is given to this aspect in the Cochrane Library Review as described above.

"Recommendations: On the whole I consider that the manuscript does not merit publication in its current form since it could mislead the readers about the success of a particular treatment (TENS and ALTENS) for a difficult problem (chronic back pain). But I would like to see the manuscript published since the 2nd message, i.e. lack of adequate studies, will perhaps prompt someone or some groups to do further research. Can I suggest a "letter to the editor" type format (e.g. as in Gemignani G. et al 1991) or as a short report (500-750 words with fewer than 10 references and perhaps with one figure)".

Action: The authors agree with these conclusions, in the light of the most unfortunate history and the time span which surrounds this paper. Appropriate changes would have been made to the text of this paper in line with the above comments but time has beaten us on this. However, appropriate changes will be made to the text of the Cochrane Review in line with the relevant observations described above. We also

prepared and submitted a "letter to the editor" type format as suggested by the referee and this also was rejected on the 25th July. The reasons given were *"As the editorial committee wrote to you, they did not think that the analysis took the debate forward sufficiently for us to offer publication in the BMJ. Unfortunately, we think that that applies to a letter as much as to a paper; you found very few studies that met your inclusion criteria, and you do not provide any hard data in the letter. We have so many letters sent to us that we can publish under a third. The authors must realise that letters are much more likely to be rejected than accepted"*. Here we must let this debate rest but we could of course make a case for publication bias in respect of this paper, or perhaps even a case for publication bias against non-medical practitioners writing for a medical journal.

However, in the meantime, we are especially pleased that the Evidence-Based Medicine Journal has recently published the said Cochrane Review, as a summarised value-added abstract, with a commentary by Professor Ernst, as discussed below.

4.6.7.2 The Evidence-Based Medicine Journal

The commentary to the Evidence-Based Medicine extract in press (July/Aug edition) by Professor Edzard Ernst, MD. PhD., Professor of Complementary Medicine is as follows:

"Given the socio-economic importance of low-back pain, it is a matter of urgency to find a treatment that really works. TENS or ALTENS is often used for this condition but their effectiveness remains uncertain. This methodologically rigorous meta-analysis suggests that TENS or ALTENS is superior to placebo in relieving pain and restoring function. Although this result looks straightforward at first glance, its practical implications are probably not. One concern is that the effect size is not large and therefore may seem unconvincing to clinicians. This fact is compounded by the paucity of studies included in the final meta-analysis. Even these few studies do not contain homogenous groups of

patients; many of those included could be classified as failed back surgery syndromes and most had non-specific low-back pain (which in itself is hardly a well-defined disease entity). The authors attempt to test several different hypotheses. To draw more reliable conclusions, a larger data set would be needed and it may, therefore, have been helpful to include studies other than those in English. There are many TENS or ALTENS studies published in French, German, Spanish, and other languages, and their inclusion might have made a difference to the conclusiveness of this meta-analysis.

As it stands, the meta-analysis may be of limited use to those who routinely treat patients with low-back pain. The authors do not comment on some of the discrepancies between their findings and the results of other systematic reviews on the subject, thus leaving the reader with an element of uncertainty on whether this intervention actually works. Clinicians need to know which treatment patients with low-back pain will benefit from which treatment modality. To find this answer is not easy, and the present meta-analysis may not offer any finite solutions in this regard. So far, the definitive study on optimal therapy for low-back pain remains elusive”.

Action: The comments by Prof. Ernst on “this rigorous meta-analysis” are acknowledged and we can understand his cautious commentary, albeit made at an early stage of publication of this evolving Cochrane Systematic Review. However, if we take into account the changes and refinements described in response to the comments and criticisms, received from the Criticisms Editor, which has strengthened rather than weakened the results of the meta-analysis, then perhaps Prof. Ernst may be more impressed with the revised conclusions to the review.

It is true that there was a paucity of studies available to the reviewers, participants with poorly differentiated diagnoses, studies of low power, and a larger data set would of course have been most welcome. However, we live in the real world and can only work with the best available evidence and this we have sought to do in this Cochrane

Review. We believe, however, that this systematic review does in fact present the best available evidence on the effectiveness of the electrical treatment of chronic back pain we have at this time, and the more so after over twenty years of inconclusive research based on single research studies have failed to provide a definitive answer.

It is also true that including non-English studies would have been helpful. It is a fact however, that no non-English studies of TENS/ALTENS for chronic back pain were identified during the initial search strategy, even though several non-English language studies were identified for other conditions. There must of course be other non-English language studies for the treatment of chronic back pain using TENS/ALTENS, as suggested by Professor Ernst, but it was beyond the means of the review team (and probably the Cochrane Collaboration too) at the time of protocol development and actual construction of this review. Their inclusion might indeed have made a difference to the conclusiveness of this meta-analysis and hopefully would have strengthened its positive results. This observation is based on the findings of Moher et al. (1996). Their findings were that no significant differences between trials published in English and other language trials were found in respect of completeness of reporting scale (randomisation), double-blinding, withdrawals or for an overall quality score. However, of interest to this review were the findings that other language trials were more likely than English-language trials to use two or more interventions and to compare two or more active treatments without an untreated control group (the essence of this review) and that trials in other languages were less likely to report a clearly prespecified primary outcome or any rationale for sample size estimation.

This study was limited to the assessment of completeness of randomisation, double-blinding, dropouts and withdrawals. It is also possible that trials published in English are more methodologically sound and explore questions of greater clinical significance (Rossetti 1993). Moher concludes that "if trials published in other languages are ex-

cluded from systematic reviews, this fact and a justification for the action should be given in the paper” and this aspect has been discussed in relation to this Cochrane Review earlier. In view of the above comments we would like to suggest that a new strategy for identifying non-English studies should be developed along the following lines:

- To establish a procedure for co-operative searching of non-English databases preferably through the network of Cochrane Centres and participating academic institutions.
- To establish an international network of specialist medical reviewers prepared to review non-English studies and to participate in Cochrane Reviews with established teams. Stressing the point of specialist medical reviewers, in the light of Sandford’s (1996) letter to *The Lancet*, which identified problems recruiting language students and ‘individuals fluent in other languages’ as translators as suggested by Moher et al (1996). She identified the difficulties rendering a study written in one language into an accurate version in another, which requires not only a thorough understanding of the source language, but also a specialist knowledge of the subject and gives some fascinating examples of error e.g. *artèrite* (peripheral occlusive artery disease) for *arteritis*, *angine* (sore throat) for *angina* etc.
- In order to achieve the second objective it would be necessary to provide appropriate training for these specialist reviewers through the Cochrane Centres and electronic media.

Clearly, a systematic review should consider all relevant trials regardless of language and as Gregoire et al (1995), identified in their study of 36 systematic reviews, that the results of one review would have been significantly different if reports in all languages had been included in the analysis. To this end we invite all readers who have knowledge of non-English language placebo controlled randomised trials of TENS/ALTENS, and who are or know of a content area expert for translation purposes, to contact Gordon Gadsby: (Email: joseph.gadsby@virgin.net) with full details and to request a set of data

the Canadian and Dutch reviews the reader is referred to our comments in the text of the review which considers their strengths and weaknesses in some detail. It is far too easy to accept a negative conclusion when this is in agreement with other published reviews and some studies, which are often seen as the gold standard (e.g. Deyo 1990), but which in fact do have biases of their own as discussed in full in the main text of this Review. Moreover, it is also far too easy to accept negative evidence to support these views and to ignore the positive evidence, which is also available. This search for all available evidence is one we have attempted to do in this review and could be one of the reasons why we have found a positive effect for TENS/ALTENS in the treatment of chronic back pain. This treatment response is also in keeping with every day clinical practice which strongly suggests that the effectiveness of TENS/ALTENS is not confined to the views and experience of practitioners but also verified by patients who seek and improve following the use of these modalities.

As the review stood at the time of Professor Ernst's commentary we would have agreed that this meta-analysis may have been of limited use to those who routinely treat patients with chronic back pain. We also believe that recent revisions and improvements to the meta-analysis, in response to comments and criticisms from the various sources, identified above, have in fact improved the level of certainty we may have in these results and these are described more fully in the text and condensed in the abstract to this review. However, having said all that, it is still essential that a powerful randomised placebo controlled trial be sought in order to confirm and strengthen once and for all the effectiveness of TENS/ALTENS in the treatment of chronic back pain in line with the findings and recommendations of this Cochrane Review.

In the final analysis, the authors would like to point out that no piece of work is ever perfect and the more it is read, the more criticism may be received. However, we believe that that even though this work has already been through the peer review process, prior to publica-

tion, the comments and criticisms section must inherently have improved this stage of a continually evolving review process within the framework of the Cochrane Collaboration.

4.6.8 Updating Reviews:

Reviewers agree to keep their registered Cochrane Reviews up-to-date. This entails repeating, at periodic intervals, the steps involved in the original review and especially the detection of new studies using appropriate search strategies, liaising with the appropriate CRG search co-ordinator and their trials register, review earlier studies if indicated by new evidence on variables not previously assessed and lastly responding to formal and informal criticism systems as discussed above.

Comment: Having considered the above comments and criticisms in some detail, the authors were now in a position to update the text of this review in the light of these observations and to repeat the steps involved in the original review, including the detection of new studies, appropriate search strategies and so on. This updating has now been completed and is shown in section 4.5 of this thesis and will be available in the Cochrane Library Issue 2 1998

4.7 Conclusions and recommendations:

This section of the thesis examined in detail the methodology and conduct of Cochrane Systematic Reviews and Meta-analyses, with detailed reference to the authors Cochrane Review under examination in this thesis

An overview of the Cochrane Collaboration, systematic reviews, and meta-analysis was given at the outset of this section, and this was followed by detailed sub-sections outlining the Cochrane Collaboration's Handbook of Guidelines for developing:

1. A Research Protocol.
2. A Cochrane Review.
3. Improving and updating these reviews.

These guidelines and their implementation in respect of the Cochrane Review under examination are then described in an original 'case-study' format.

The full published edition of the Cochrane Review is also included (4.5), extracted from its original Cochrane Library Format into Word97 format of this thesis, as "The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain. A Cochrane Library Review (Gadsby and Flowerdew 1997).

Improving and updating this Cochrane Review, on the lines indicated in the thesis text, will continue on an ongoing basis during the completion stages of this thesis and its subsequent submission for academic examination for the degree of Doctor of Philosophy and thereafter for an unspecified period of time.

The final section (5) of this thesis follows as an evaluation of the contribution this research study programme, conducted over the last six years, makes to our knowledge base in respect of the historical and contemporary development of electroanalgesia and the evidence-base which is now available to support the use of TENS and ALTENS treatments for chronic low back pain.

5.

**Conclusions and the
contribution this
thesis makes to our
knowledge base**

5.0 The contribution this thesis makes to our knowledge base and final conclusions.

5.1 Introduction:

This final section of this thesis examines the contribution to our knowledge base this six-year programme of study makes. It begins with a review of each section of the thesis and the conclusions drawn from it. A listing of the relevant publications for each section follows. In the final analysis the overall conclusions for this programme of study are drawn together and presented in summary.

5.2 Section 3. Historical and Experimental Studies:

This section sets the scene with an in-depth examination of the electroanalgesia literature, both historical and contemporary, together with a history of medicine study on the Rev. John Wesley as a pioneer electrotherapist. This was followed by a clinical research study of electroanalgesia in palliative medicine, designed to help both the dying patient and to enable the researcher gain first hand experience in the research method. The initial stage of the thesis was designed in order to lay down a solid basis for the Ph.D. research stage in respect of the following areas:

1. An examination of the historical background of electroanalgesia from early times to the present day (3.2).
2. A history of medicine case study focussing in on electroanalgesia and the establishment of an alternative/complementary medical system in the eighteenth-century (which also holds many similarities to the present trend for alternative and complementary therapies, i.e. as a reaction to some of the heroic measures of orthodox medicine at the time) by the eighteenth-century divine and pioneer electrotherapist – The Rev. John Wesley MA (see 3.3). This study also examined John Wesley's unique contribution to holistic health

care in body, mind, spirit, and social aspects of health, with special emphasis on his electrotherapy techniques. A consideration of the relevance and implications of his work both for the present and for the future followed this. The main aim of this study then, was to present a fresh interpretation of John Wesley's eighteenth-century whole person healing ministry, in the light of the rapid development of holistic and alternative and complementary medicine in the last decade of the twentieth century. I also set out to demonstrate the relevance of John Wesley's life and work for all interested parties, but especially for those interested in the current and future practice and research of holistic medicine, electrotherapy, and evidence-based orthodox and alternative and complementary medicine as we rapidly approach the twenty-first century.

An examination of the biological and electrical mechanisms of pain and electrical pain relief (see 3.4 and 3.5 respectively). The third stage of this historical and experimental review was to evaluate the basic mechanisms of pain and to establish the accepted electrical parameters of electro-analgesia from the available published literature. This was necessary at this stage of the research in order to establish the scientific bases of electroanalgesia, still apparently misunderstood by many in the light of their own studies (examined in section 4.5), in preparation for conducting the clinical research project and also to strengthen the foundations for the doctoral stage of tertiary research as systematic review and meta-analysis.

3. An electroanalgesia clinical research study - as a placebo controlled randomized controlled trial of acupuncture-like transcutaneous electrical nerve stimulation in palliative medicine (see 3.5). This randomised controlled study was designed with the aims of helping the dying patient in the following areas of palliative medicine:
 - i. to improve pain relief,
 - ii. to control nausea and vomiting,
 - iii. to improve general fatigue symptoms

- iv. and to improve the overall quality of life with the aid of a well-designed and rigorous trial methodology.

The findings from this study hold promise for the future palliative treatment of terminally ill patients and for future researchers who may wish to build on these findings, or to use the methodology of this trial as a model for those researchers who wish to examine the therapeutic effect of a treatment, over and above that, of the placebo effect (section 3.6).

It was anticipated, at the outset of this programme of study, that a full randomised controlled trial would be conducted at the Ph.D. stage, but this was not possible due to the medical politics of the situation at the time. In the meantime, the founding and development of the Cochrane Collaboration suggested a new way forward by tertiary research using systematic review and meta-analysis in the form of a Cochrane Review.

5.2.1 Publications listed to section 3.3 and 3.6:

The following publications stemmed from this section of the research programme, with the **main** author of multi-authored papers being J.G. Gadsby, with contributions from the named co-authors, and contribute to our knowledge base in written media as:

GADSBY, J.G. (1996) Rev. John Wesley MA: Holistic healing, electrotherapy and complementary medicine. Loughborough, Teamprint, 56pps. £3.00.

The above book was also indexed in FIELD, C.D. (1996) Bibliography of Methodist Historical Literature (1996). Supplement to the Proceedings of the Wesley Historical Society, May 1997, Contribution to Science and Medicine p.70. All profits from this book were donated to the Methodist Ministers Housing Association and running at just over £250 at the time of thesis writing.

GADSBY, J.G. and RICHARDSON S.Y. (1997) John Wesley – Whole Person Healer. Heritage: The Journal of the East Midlands Branch of the Wesley Historical Society, Vol 5(1), pp.2-18.

FRANKS, A., JOHNSON, I., GADSBY, J.G., JARVIS, P. and DEWHURST, F. (1996) Abstract: Acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) within palliative medicine: A pilot study. Palliative Medicine, Vol. 10, p.78.

GADSBY, J.G., FRANKS, A., JARVIS, P. and DEWHURST, F. (1997) Acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) within palliative medicine: A pilot study. Complementary Therapies in Medicine Vol 5(1), pp.13-18.

GADSBY, J.G. and DEWHURST, F. (1998) The Reverend John Wesley's contribution to the evolution of alternative and holistic healing. Epworth Review. In press.

This stage of the thesis generated three publications in respect of the history of medicine study on 'The Rev. John Wesley MA: Holistic healing, electrotherapy and complementary medicine', and two publications in respect of the randomised controlled trial on 'Acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) within palliative medicine: A pilot study', as listed above.

Comments: Considerable interest has also been generated by the book on the Rev. John Wesley MA among leading Wesleyian academics including:

Dr Henry D Rack, Bishop Fraser Senior Lecturer in Ecclesiastical History, University of Manchester who wrote to the author, "this must be the one of the most comprehensive reviews of the subject, quite apart from the discussion of the holistic theme and it is good to have so much useful information in one place"; Dr John Vickers and

leading members of the Wesley Historical Society; Dr John Cule, University of Wales College of Medicine, Medical History Unit; The Methodist Ministers Housing Society Officers; The Bakken Museum of Electricity in Life, Minneapolis, USA who requested copies for their Library; Tim Macquiban, Director of the Wesley and Methodist Studies Centre, Westminster College Oxford University, Oxford UK; Professor Randy L. Maddocks, University of Sioux Falls, South Dakota; Rev Dr Richard G. Jones, editor of the academic journal "The Epworth Review" who wrote to the author "Many thanks for sending me the fascinating article on John Wesley and his contribution to holistic medicine, most of which I did not know".

5.3 Section 4. Tertiary Research:

This section of the thesis constitutes the doctoral stage of the programme of study as tertiary research in the form of a Cochrane systematic review and meta-analysis of the effectiveness of transcutaneous electrical nerve stimulation for the treatment of chronic low back pain.

The first part of this section begins with an introduction to the programme of study for systematic reviews and meta-analysis.

The second part of this section is an examination of the literature on the conduct of systematic reviews, meta-analysis and the development of the Cochrane Collaboration (4.2) and is also a review of the main areas covered by the Cochrane Collaboration Handbook (Mulrow CD, Oxman AD (eds.) (1997)) and the Cochrane Collaboration Information Booklet (1997) in order to provide the remaining background information for the rest of the research programme.

The third part of this second section, "Developing a protocol for a Cochrane Review" (4.3), of the thesis is structured on, and is also a

summary of, the following sections from the Cochrane Collaboration Handbook: the 'Introduction', 'Formulating the problem', and 'Developing a protocol' (Mulrow and Oxman 1997). Supplementary material is also given in order to expand the utility of these guidelines, using a 'case study' approach based on the Cochrane Review under examination, and follows each main subsection summarised from the Cochrane Collaboration Handbook. The supplementary material is in the form of an application commentary, which outlines the authors' use of these guidelines in the construction of the Cochrane Review protocol. It is suggested that these expanded guidelines, and the ones included in sections 4.4 and 4.6, may be of considerable help to new reviewers joining the Cochrane Collaboration, especially those working in some isolation. To this end, these three sections will be offered to the Cochrane Collaboration as a training resource following academic examination at the doctoral level. This section ends with a full copy of the protocol for the review on 'The effectiveness of TENS and ALTENS in chronic low back pain' which was constructed in accordance with the basic guidelines in operation at the time (1994/5) of its creation.

The fourth part of this section "Developing a Cochrane Systematic Review and Meta-analysis" (4.4) is structured on, and is a summary of, the following sections from the Cochrane Collaboration Handbook: 'Format of a Cochrane review', 'Locating and selecting studies', 'Critical appraisal of studies', 'Collecting data', 'Analysing and presenting results', and 'Interpreting results', (Mulrow and Oxman 1997). Supplementary material, again using a similar 'case study' approach as described above, follows each main subsection summarised from the Cochrane Collaboration Handbook, in the form of an application commentary outlining the authors' use of these guidelines in the construction of the Cochrane Review under consideration in this thesis. Again similar comments regarding the utility of these expanded guidelines for Cochrane Collaboration, and other reviewers, are suggested here.

The fifth part of this section consists of the complete, original and most recently updated version of the Cochrane Review, "The effectiveness of Transcutaneous Electrical Nerve Stimulation (TENS) for chronic low back pain – A Cochrane Library Review (4.5). The structure includes the full text, tables and charts, and is extracted from the RevMan software prior to submission for inclusion in the next edition of the Cochrane Library on CD-ROM due in April 1998. The review under discussion is the first of many reviews currently under consideration by the back subgroup of the Musculoskeletal Group of the Cochrane Collaboration but it is the **first and only review** (entered into the Cochrane Library, January 1997) in this section of the Cochrane Library at the time of writing (January 1998). This review finally demonstrates that effective clinical benefits are to be found in the use of ALTENS/TENS for chronic low back pain, at least in the short term, this assessment being based on the best available evidence we have at this time (1998). Furthermore, it is an inexpensive and cost effective therapeutic measure with very few adverse outcomes. There may be inconclusive evidence on the long-term beneficial effects i.e. 'no evidence of effect' at this stage in our knowledge rather than there being 'evidence of no effect'.

This review goes on to suggest a way forward in the form of a definitive research study to confirm, strengthen and consolidate the last twenty-five years of research – once and for all as described in the conclusion section of the review. This is necessary in order to move the interventions of ALTENS and TENS on from 'the category of care for which there is insufficient evidence to provide clear guidelines for practice' to 'forms of care for which there is sufficient evidence to provide clear guidelines for practice'.

The sixth part of this section, "Improving and Updating Systematic Reviews using the Cochrane Collaboration 'Comments and Criticisms' mechanism" (4.6), is also structured on, and is a summary of, the fol-

lowing section from the Cochrane Collaboration Handbook: 'Improving and Updating Reviews', (Mulrow and Oxman 1997). Supplementary material, again using a 'case study' approach, in the form of an application commentary/action taken, outlines the authors' use of these guidelines in improving and updating the Cochrane Review under consideration in this thesis and the same comments apply to this part as to those described in parts 4.3, and 4.4 in respect of their utility for/by interested reviewers.

Having considered the comments and criticisms described in some detail in the text of (4.6), the authors were now in a position to update the text of this review in the light of these observations and to repeat the steps involved in the original review, including the detection of new studies, appropriate search strategies and so on. This updating is now complete as described in section 4.5 and will be available to a wider readership through the next edition of the Cochrane Library (April 1998).

5.3.1 Publications listed to section 4:

The following publications stemmed from this section of the research programme, with the **main** author of multi-authored papers being J.G. Gadsby, apart from equal co-authorship for the paper (Flowerdew and Gadsby 1997), (and comments/agreement only to the Evidence-Based Medicine Journal abstract) with contributions from the named co-authors in other papers, and contribute to our knowledge base both by written and electronic media as:

GADSBY JG, FLOWERDEW MW, (1998) The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain. In: Bombardier C, Nachemson A, Deyo R, de Bie R, Bouter L, Shekelle P, Waddell G, Roland M, and

Guillemin F (Eds.) CMSG Back Module of The Cochrane Database of Systematic Reviews, [updated January 1998]. Available in the Cochrane Library [database on disk and CDROM]. The Cochrane Collaboration; Issues 1 and 2. Oxford: Update Software; 1998. Updated quarterly.

GADSBY G, FLOWERDEW MW, (1997) Nerve stimulation for low back pain – a review. Nursing Standard, Vol 43(11), pp32-3.

GADSBY JG, FLOWERDEW MW, (1997): Review: Transcutaneous electrical nerve stimulation reduces pain and improves range of movement in chronic low-back pain **[Abstract]**. Evidence-Based Medicine. 1997 July-Aug, 2(4): Abstract of GADSBY JG, FLOWERDEW MW, (1997) The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain. In: Bombardier C, Nachemson A, Deyo R, de Bie R, Bouter L, Shekelle P, Waddell G, Roland M, and Guillemin F (Eds.) CMSG Back Module of The Cochrane Database of Systematic Reviews, [updated 22 May 1997]. Available in the Cochrane Library [database on disk and CDROM]. The Cochrane Collaboration; Issue 3. Oxford: Update Software; 1997. Updated quarterly.

FLOWERDEW MW, GADSBY JG, (1997) A review of the treatment of chronic low back pain with acupuncture-like transcutaneous electrical nerve stimulation and transcutaneous electrical nerve stimulation. Complementary Therapies in Medicine, Vol. 5(4), pp.193-201.

5.4 The Contribution this thesis makes to Evidence-Based Health Care.

Whilst it was not one of the original objectives of this thesis to consider the contribution this programme of study might make to evidence-based health care (EBHC), it became increasingly apparent as the work progressed, and as the principles of evidence-based medicine

(EBM) became more widely published, that this study does have an important contribution to make and the decision was therefore made to include and discuss this contribution to our knowledge base in this part of the thesis.

Evidence-based medicine, whose philosophical origins extend back to mid-19th century Paris and earlier, is *"the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients coupled with the integration of individual clinical expertise i.e. the proficiency and judgement that individual clinicians acquire through clinical experience and practice"* (Sackett 1996/1997b).

This set of evolving principles, strategies and tactics, which have become known as 'evidence-based health care', include scientific methods for studying patients and populations, e.g. the randomised controlled trial; means for tracking down, critically appraising, and synthesising this evidence e.g. the systematic review; together with the rigorous evaluation of the precision and accuracy of clinical examinations, and the sensitivity, specificity and utility of diagnostic investigations, have been pioneered in Oxford and other leading health sciences centres around the world. The recently established Oxford Centre for Evidence-Based Medicine now contributes to further development through applied research, translation of research results into clinically-useful tools and ways of thinking, e.g. the number of patients needed to be treated to prevent one event, and helps health professionals learn how to apply these principles in the front line (Sackett 1997a/b).

Evidence-Based Health Care extends the principles, strategies and tactics of evidence-based decision-making to other health professionals e.g. physiotherapists, nurses, dentists and to alternative and complementary practitioners too. So how does the author's programme of research described in this thesis fit in with the objectives of

EBHC? The author's programme of study contains the following elements of evidence that make a contribution to the practice of EBHC within both orthodox and alternative and complementary medicine.

1. Whilst the initial stages of the thesis concentrates on building up the background information to support the doctoral stage, there is a contribution to evidence-based health care in the form of the randomised controlled trial described in section 3.6. This study was accepted for publication on the basis of the trial methodology, rather than the results of the study, which suggests that other trialists may wish to consider this approach in more detail. Moreover, the results of this study also suggest that beneficial effects may be obtained from the use of acupuncture-like transcutaneous electrical nerve stimulation within palliative medicine. The three most important and debilitating symptoms within palliative care, pain, nausea and vomiting and fatigue were examined and the study showed some clinical improvements in the last two, which would warrant further investigation in the future.

2. The doctoral stage of the research programme contributes to Evidence-Based Health Care in the following ways:

- a. An examination of the methodology and development of systematic reviews, from the researcher's viewpoint, including an appraisal of systematic review guidelines and a critique of the peer review process, designed to provide background knowledge and help for other reviewers especially new collaborators and those working in some isolation.
- b. Developing a protocol for a Cochrane Systematic Review with a discussion on the recommended guidelines again designed to help new reviewers.
- c. Developing a Cochrane Systematic Review and Meta-analysis with a discussion on the recommended guidelines again designed to help new reviewers.

- d. Completing a Cochrane Systematic Review and Meta-analysis on the effectiveness of transcutaneous electrical nerve stimulation for chronic low back pain. This study became the first Cochrane Review to be accepted into the Musculo-skeletal Back-subgroup section and bridges the divide between orthodox physical treatment (TENS) and alternative/complementary therapy (ALTENS) and became a first in this arena.
- e. The Cochrane Review under consideration also meets the inclusion criteria for publication as a structured extract and commentary in the Evidence-Based Medicine Journal (1997). The Commentary on the author's review in Evidence-Based Medicine was provided by Professor Edzard Ernst, Professor of complementary Medicine, University of Exeter, England UK. Calculations were made by the journal reviewers of the number of patients that needed to be treated (NNT) with TENS or ALTENS in order to cause one good event (i.e. reduction in low back pain) translated into 5 patients (95%CI: 3, 14) and the NNT with ALTENS to cause an improvement in the range of motion of back pain subjects was 3 patients (95%CI: 2, 5).
- f. Finally, the systematic review under examination, "The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain", provides the first statistically significant evidence, albeit from the limited data available, that TENS/ALTENS reduces pain and improves range of motion in chronic back pain patients, at least in the short term. There is also statistically significant evidence from pooling the TENS/ALTENS data in a cumulative meta-analysis (see Appendix B (iv)) to indicate that using TENS/ALTENS for the treatment of chronic low back pain could have been shown to be beneficial almost twenty years ago. These results also suggest a powerful and definitive randomised controlled trial of TENS/ALTENS is now needed to confirm these findings, once and for all, and this would also help to convince those clinicians who

still have some difficulty accepting this evidence, including some members of the Cochrane Musculoskeletal Group: Back-subgroup Editorial Committee.

5.5 On Reflection

This programme of research may be viewed as a wide ranging study of electro-analgesia with the main emphasis on tertiary research and an evaluation of the electrical treatments of TENS and ALTENS for chronic back pain patients. This subject is especially important for the 10% of acute back pain sufferers who progress to this chronic stage and for practitioners who are involved in their treatment. There are many treatments for chronic back pain, most (if not all) of which have not yet been validated as effective by high quality research. I see this systematic review and meta-analysis as being the first of many studies aimed to rectify this situation and to establish evidence-based health care in this most important area of care. On reflection, it might have been easier for the author to have chosen a less difficult subject to review, e.g. migraine, trigeminal neuralgia or post herpetic neuralgia etc, with fewer studies to consider. However the author remains convinced that the correct decision was made to examine the electrical treatment of chronic low back pain in detail using the methodology of the Cochrane Collaboration and its supporting structures.

The methodology of this systematic review followed the guidelines laid down in the first edition of the Cochrane Handbook, and even though these have now been reviewed, the main elements have not changed greatly and this review will withstand appraisal from the basis of these new guidelines. In retrospect, it would have been most helpful, however, if guidelines for assessing the quality of individual trials, using a validated scoring method, had been available at the outset rather than as a post-hoc requirement of the editorial process. It would also have been useful at the outset to establish the numbers

of studies in non-English languages and to seek their translation and assessment. However, the initial search strategy had failed to uncover any non-English language publications for inclusion in this systematic review even though Professor Ernst suggests that there are still many studies in Spanish, French and German languages available for review. If this is true, which I somewhat doubt following a second intensive search strategy at the end of 1997, especially of the European EMBASE database for non-English language publications, which again failed to identify any non-English language studies relating to chronic back pain, then perhaps it may have affected the results of this Cochrane Review in some way. It could also be argued, however, that if high quality non-English randomised controlled trial studies were available then perhaps they would also have been published in the English language, or at least be referenced in the major medical databases or individual study bibliographies, searched for this review.

There were very few problems encountered during the review process itself perhaps due to the dedication of my co-reviewers. It was unfortunate, however, that Professor Alan Bennett had to withdraw from the review process, after the initial assessment had been completed. This was due to commercial circumstances not related in any way to the conduct of this review. It was perhaps fortunate for the author that he had selected two content area expert reviewers to assist him in this process – so all was not lost.

The process of systematic review and meta-analysis can be a long and tedious process, especially if there are many studies to read and review, e.g. 70 in this study, and even more so if there are many of poor methodological quality. It is also a sad reflection on the poor quality of most of the research papers read for this review, a problem which also seems to be universal to most studies identified by reviewers, and one which will hopefully resolve with future high quality research programmes.

In the final analysis the results of this systematic review and meta-analysis confirmed, albeit from the limited evidence that was eventually available, that the use of electrical therapies, as TENS and ALTENS, were effective in reducing the levels of pain and that ALTENS improved the range of motion in chronic back pain subjects. These results confirmed our clinical experience, having using these treatment over the past twenty years, but we were somewhat surprised that the strength of the treatment effect, over and above that of placebo, was not higher than the meta-analysis showed. However, these results led us to the suggestion that a definitive placebo controlled randomised trial is still needed to convince the sceptics among us that the results of the review are correct.

Even though we played by the rules of the game, it is still difficult to convince practitioners and some editorial group members, who perhaps fix on one randomised controlled trial with a negative outcome, i.e. in this case Rick Deyo's study, and then refuse to accept that a positive outcome is a distinct possibility, even when the flaws in this negative trial have been examined and reported by the reviewers and by other practitioners as discussed in the text. It is to be hoped, however, that the inclusion of this review in the evidence-based medicine journal will help to overcome this prejudice in the fullness of time.

In hindsight, would I now set out on this path again? The answer is of course, yes, for there are so many areas of health care, both orthodox and alternative/complementary to be evaluated in order to produce the evidence-base which so many of us are seeking. Whilst I may not be able to participate in as many of these systematic reviews as I would wish, as an independent practitioner not attached to an academic centre, nonetheless it is my hope for the future that I may be able to help others in some way in this great task ahead of us.

5.6 In Conclusion

This final section of the doctoral thesis has examined in detail the results of this historical and contemporary investigation into electroanalgesia and the contribution to knowledge that has ensued. The research programme, culminating in tertiary research as a systematic review and meta-analysis and a cumulative meta-analysis, shows for the first time ever, statistically significant clinical effects of electrical stimulation, as TENS and ALTENS, in the treatment of chronic low back pain patients and that we can now reject the null hypothesis of no treatment effect.

Furthermore, if these approaches were implemented on a global basis, then considerable numbers of chronic low back pain sufferers would benefit with a reduction in their levels of pain and discomfort.

Finally, by using ALTENS treatments, in preference to conventional TENS treatment, this regime would also increase the range of motion of these patients, thereby improving their overall quality of life in a non-invasive and cost-effective way.

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